

## IPKPYPP PJPbP|P+PI

**P+P»C PjPµPrPëC±PSPsPiPs P·P°CÍC,PsCÍCíPIP°PSPSC P»C-PeP°CÍCHbPePsPiPs P·P°CÍPsP±Cí**

**PkP+PyPhPµP+Pk**

**(NITOPIN<sup>B®</sup>)**

**PYPeP»P°Pr:**

*PrC-CHC±P° C PµC±PsPIPëPSP°: nimodipine;*

1 C,P°P±P»PµC,PeP°, PIPeC PëC,P° PìP»C-PIPePsPIPsC P±P±PsP»PsPSPePsC, PjC-CÍC,PëC,CH PSC-PjPsPrPëPìC-PSCí 30 PjPi;

*PrPsPìPsPjC-P PSC- C PµC±PsPIPëPSPë: C+PµP»CHP»PsP·P° PjC-PeC P±PeC PëCÍC,P°P»C-C±PSP°, PeC P±C...PjP°P»CH PeCíPeCíCíPrP·C PSPëPN, PìPsP»C-PIC-PrPsPS, PeC P±CíPìPsPIC-PrPsPS, PjP°PiPSC-C CÍC,PµP°C P°C,;*

*PsP±PsP»PsPSPeP°: PiC-PìC P±PjPµP»PsP·P°, PjP°PeC P±PiPsP» 4000, C,PëC,P°PSCí PrC-PsPeCíPëPr (E 171).*

**P»C-PeP°CÍCHbPeP° C,,PsC PjP°. PYP°P±P»PµC,PePë, PIPeC PëC,C- PìP»C-PIPePsPIPsC P±P±PsP»PsPSPePsC.**

*PhCÍPSPsPIPS- C,,C-P·PëPePs-C...C-PjC-C±PSC- PIP»P°CÍC,PëPIPsCÍC,C-: P±C-P»C- P°P±Ps P P±PIC,CíPIP°C,C- PrPIPsP±CíPeP»C- C,P°P±P»PµC,PePë.*

**P»P°C PjP°PePsC,PµC P°PìPµPIC,PëC±PSP° PiC CíPìP°.**

*PYPµP»PµPeC,PëPIPS- P±P»PsPeP°C,PsC Pë PeP°P»CHC+C-C"PIPëC... PeP°PSP°P»C-PI P· PìPµC PµPIP°P PSPëPj PìPìP»PëPIPsPj PSP° CÍCíPrPëPSPë. PµPsC...C-PrPSC- PrPëPiC-PrC P±PiC-C PëPrPëPSCí. PkC-PjPsPrPëPìC-PS.*

*PµPsPr PhPyPI C08C A06.*

**P»P°C PjP°PePsP»PsPiC-C±PSC- PIP»P°CÍC,PëPIPsCÍC,C-.**

*P»P°C PjP°PePsPrPëPSP°PjC-PeP°.*

*PkC-PjPsPrPëPìC-PS C" P±P»PsPeP°C,PsC P±Pj PeP°P»CHC+C-C"PIPëC... PeP°PSP°P»C-PI PrPëPiC-PrC P±PiC-C PëPrPëPSPsPIPsC— PiC CíPìPë P· PìPµC PµPIP°P PSPëPj PìPìP»PëPIPsPj PSP° CÍCíPrPëPSPë PìPsP»PsPIPSsPiPs PjPsP·PeCí. PkC-PjPsPrPëPìC-PS P·P±C-P»CHC CíC"*

C†PμCḡPμP±CḡP°P»CHPSCř PīPμCḡC,,CřP·C-Cḡ, P·PsPeCḡPμPjP° PI PrC-P»CłPSPeP°C... C-P· PīPsPiC-CḡC€PμPSPsCḡ PīPμCḡC,,CřP·C-CḡCḡ, C€P»CłC...PsPj CḡPsP·C€PēCḡPμPSPSCł P°CḡC,PμCḡC-PNē. PīPμPNē PμC,,PμPeC, PīCḡPsPīPsCḡC†C-PNēPSPs P±C-P»CHC€PēPNē Cř PjPμPSC€PēC... CłCřPrPēPSP°C..., PSC-P¶ Cř P±C-P»CHC€PēC....

P' CřPjPsPIP°C... *in vitro* PIP°P·PsPePsPSCłC,CḡPēPeC†C-Cḡ, CłPīCḡPēC†PēPSPμPSCř CḡC-P·PSPēPjPē PIP°P·PsP°PeC,PēPIPSPēPjPē CḡPμC†PsPIPēPSP°PjPē (PSP°PīCḡPēPeP»P°Pr CłPμCḡPsC,PsPSC-PS, PīCḡPsCłC,P°PiP»P°PSPrPēPS C,P° PiC-CłC,P°PjC-PS) P°P±Ps PīCḡPμPīP°CḡP°C,P°PjPē PeCḡPsPIC- C,P° PīCḡPsPrCřPeC,P°PjPē CḡPsP·PīP°PrCř PeCḡPsPIC-, PIPrP°PIP°P»PsCłCł PīPsPīPμCḡPμPrPēC,Pē P°P±Ps P·PjPμPSC€PēC,Pē (PrPs 75 %) P·P°CłC,PsCłCřPIP°PSPSCłPj PSC-PjPsPrPēPīC-PSCř.

*PαP°CḡPjP°PePsPeC-PSPμC,PēPeP°.*

PμC-CłP»Cł PīPμCḡPsCḡP°P»CHPSPsPiPs P·P°CłC,PsCłCřPIP°PSPSCł P»C-PeP°CḡCłCHPePēPNē P·P°CłC-P± C€PIPēPrPePs PICłPjPsPeC,CřCḡC,CHCłCł. PḡP°PeCłPēPjP°P»CHPSP° PePsPSC†PμPSC,CḡP°C†C-Cł Cř PīP»P°P·PjC- PeCḡPsPIC- CłPīPsCłC,PμCḡC-PiP°CḡC,CHCłCł C†PμCḡPμP· 30Bḡ“60 C...PI PīC-CłP»Cł PīPμCḡPsCḡP°P»CHPSPsPiPs P·P°CłC,PsCłCřPIP°PSPSCł. PkPμP·PIP°P¶P°CḡC†Pē PSP° PIPēCłPsPeCř C€P»CřPSPePsIPs-PePēC€PePsPICř P°P±CłPsCḡP±C†C-Cḡ PSC-PjPsPrPēPīC-PSCř, P°P±CłPsP»CḡC,PSP° P±C-PsPrPsCłC,CřPīPSC-CłC,CH CłC,P°PSPsPIPēC,CH 5Bḡ“15 %, C%Ps PīPsCłCłPSCḡCḡC,CHCłCł PμPeCłC,PμPSCłPēPIPSPēPj PīCḡPμCłPēCłC,PμPjPSPēPj PjPμC,P°P±PsP»C-P·PjPsPj (P±P»PēP·CHPePs 85Bḡ“95 %).

P PsP·CḡP°C...PsPIP°PSPēPNē PsP±Bḡ™CḡPj CḡPsP·PīPsPrC-P»Cř (Vss, PrPIPpsPeP°PjPμCḡPSP° PjPsPrPμP»CH) PīCḡPē PIPSCřC,CḡC-C€PSCḡPsPIPμPSPSPsPjCř PIPiPμPrPμPSPSC- PrPsCḡC-PIPSCḡC” 0,9Bḡ“2,3 P»/PePi PjP°CłPē C,C-P»P°. P—P°PiP°P»CHPSPēPNē (CłPēCłC,PμPjPSPēPNē) PeP»C-CḡPμPSCł CłC,P°PSPsPIPēC,CH 0,8Bḡ“1,6 P»/PiPsPr/PePi. PkC-PjPsPrPēPīC-PS PSP° 97Bḡ“99 % P·PiBḡ™CłP·CřCḡC,CHCłCł P· P±C-P»PeP°PjPē PīP»P°P·PjPē PeCḡPsPIC-.

PḡPμC,P°P±PsP»C-C†PSPμ PIPēPrP°P»PμPSPSCł PSC-PjPsPrPēPīC-PSCř P·PrC-PNēCłPSCḡCḡC,CHCłCł PīPsP»PsPIPSPēPj C†PēPSPsPj CłPēCłC,PμPjPsCḡ C†PēC,PsC...CḡPsPjCř P450 3A4. PkC-PjPsPrPēPīC-PS PIPēPIPpsPrPēC,CHCłCł Cř PIPēPiP»CłPrC- PjPμC,P°P±PsP»C-C,PI, C%Ps CřC,PIPSCḡCḡC,CHCłCł PīPμCḡPμPIP°P¶PSPs C€P»CłC...PsPj PrPμPiC-PrCḡPsPiPμPSC-P·P°C†C-C— PrPēPiC-PrCḡPsPiC-CḡPēPrPēPSPsPiPs PeC-P»CHC†Cł C,P° PsPePēCłPSPsPiPs Ph- PrPμPjPμC,PēP»CHPIP°PSPSCł. PhPePēCłPSPμ CḡPsP·C%PμPīP»PμPSPSCł PμC,,C-CḡCř, PiC-PrCḡPsPeCłPēP»CHPIP°PSPSCł 2- C,P° 6-PjPμC,PēP»-PiCḡCřPi C,P° PīP»CHPeCřCḡPsPSC-P·P°C†C-Cł CłPe CḡPμP°PeC†C-Cł PePsPSBḡ™CḡPiP°C†C-C— C” PSP°CłC,CřPīPSPēPjPē PIP°P¶P»PēPIPēPjPē P»P°PSPeP°PjPē PjPμC,P°P±PsP»C-P·PjCř. PḡCḡPē PsCłPSPsPIPSC- PjPμC,P°P±PsP»C-C,Pē, PIPēP·PSP°C†PμPSC- Cř PīP»P°P·PjC- PeCḡPsPIC-, PSPμ PIPēCłPIPēP»Pē P°P±Ps PIPēCłPIPēP»Pē P»PēC€Pμ PSPμP·PSP°C†PSCř P·P°P»PēC€PePsPICř C,PμCḡP°PīPμPIC,PēC†PSCř P°PeC,PēPIPSC-CłC,CH.

PkPμ PIPēCłPIP»PμPSPs C-PSPrCřPeCřCḡC†PsC— P°P±Ps C-PSPiC-P±CřCḡC†PsC— P°PeC,PēPIPSPsCłC,C- C%PsPrPs C,,PμCḡPjPμPSC,C-PI PīPμC†C-PSPePē. P'PēPIPμPrPμPSPSCł PjPμC,P°P±PsP»C-C,PI Cř P»CHPrPēPSPē P·PrC-PNēCłPSCḡCḡC,CHCłCł PSP° 50 % PSPēCḡPeP°PjPē C,P° PSP° 30 % C-P· P¶PsPIC†Cḡ.

PμCḡPē PīPμCḡPsCḡP°P»CHPSPsPjCř P·P°CłC,PsCłCřPIP°PSPSC- PjP°PeCłPēPjP°P»CHPSP°

PePsPSC†PμPSC, CḡP°C†C-Cḡ Cr PīP»P°P·PjC- PeCḡPsPIC- C,P° PīP»PsC%P° PīC-Pr  
PeCḡPēPIPsCḡ B«PePsPSC†PμPSC, CḡP°C†C-Cḡ-C‡P°CḡB» P·CḡPsCḡC,P°CḡC,CH  
PīCḡPsPīPsCḡC†C-PN°PSPs PrPsP·C- P°Pḡ PrPs PSP°PN°PIPēC%PsC—  
PrPsCḡP»C-PrPḡCḡPIP°PSPsC— PrPsP·Pē (90 PjPi). PḡC-PSPμC,PēPeP° PIPēPIPμPrPμPSPSCḡ C”  
P»C-PSC-PN°PSPsCḡ. PμPμCḡC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCḡ PSC-PjPsPrPēPīC-PSCḡ  
CḡC,P°PSPsPIPēC,CH PIC-Pr 1,1 PrPs 1,7 PiPsPrPēPSPē. PḡPμCḡPjC-PSP°P»CHPSPēPN°  
PīPμCḡC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCḡ 5Bḡ“10 PiPsPrPēPS PSPμ C”  
CḡPμP»PμPIP°PSC,PSPēPj PrP»Cḡ PICḡC,P°PSPsPIP»PμPSPSCḡ  
CḡPμPePsPjPμPSPPrPsPIP°PSPsPiPs C-PSC,PμCḡPIP°P»Cḡ PjC-Pḡ PīCḡPēPN°PsPjPsPj PrPsP·  
P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ.

**PḡP»C-PSC-C‡PSC- C...P°CḡP°PeC,PμCḡPēCḡC,PēPePē.**

**PμPsPeP°P·P°PSPSCḡ.**

PμCḡPsC,,C-P»P°PeC,PēPeP° C,P° P»C-PeCḡPIP°PSPSCḡ C-CēPμPjC-C‡PSPēC...  
PSPμPICḡPsP»PsPiC-C‡PSPēC... CḡPsP·P»P°PrC-PI PīC-CḡP»Cḡ  
CḡCḡP±P°CḡP°C...PSPsC—PrP°P»CHPSPsPiPs PeCḡPsPIPsPIPēP»PēPICḡ PIPSP°CḡP»C-PrPsPe  
CḡPsP·CḡPēPICḡ P°PSPμPICḡPēP·PjPē.

**PμCḡPsC,PēPīPsPeP°P·P°PSPSCḡ.**

PμC-PrPIPēC%PμPSP° C‡CḡC,P»PēPIC-CḡC,CH PrPs PSC-PjPsPrPēPīC-PSCḡ P°P±Ps PrPs  
C-PSCēPēC... PePsPjPīPsPSPμPSC,C-PI P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ.

PμC-Pr C‡P°Cḡ C,P° PIPīCḡPsPrPsPIPḡ PsPrPSPsPiPs PjC-CḡCḡC†Cḡ PīC-CḡP»Cḡ  
C-PSC,,P°CḡPeC,Cḡ PjC-PsPeP°CḡPrP° P°P±Ps PμPīC-P·PsPrCḡ PSPμCḡC,P°P±C-P»CHPSPsC—  
CḡC,PμPSPsPeP°CḡPrC-C—.

P—P°CḡC,PsCḡCḡPIP°PSPSCḡ Cr PePsPjP±C-PSP°C†C-C— P· CḡPēC,,P°PjPīC-C†PēPSPsPj P°P±Ps  
PīCḡPsC,PēPμPīC-P»PμPīC,PēC‡PSPēPjPē P·P°CḡPsP±P°PjPē (C,,PμPSPsP±P°CḡP±C-C,P°P»,  
C,,PμPSC-C,PsC—PS, PeP°CḡP±P°PjP°P·PμPīC-PS) C‡PμCḡPμP· P·PSP°C‡PSPμ  
P·PSPēPḡPμPSPSCḡ PμC,,PμPeC,PēPIPsCḡC,C- P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ  
PḡC-C,PsPīC-PS (PrPēPI. CḡPsP·PrC-P» B«P·P·P°C”PjPsPrC-Cḡ P· C-PSCēPēPjPē  
P»C-PeP°CḡCḡCHPePēPjPē P·P°CḡPsP±P°PjPē C,P° C-PSCēC- PIPēPrPē PIP·P°C”PjPsPrC-PN°B»).

**P°P·P°C”PjPsPrC-Cḡ P· C-PSCēPēPjPē**

**P»C-PeP°CḡCḡCHPePēPjPē P·P°CḡPsP±P°PjPē C,P°**

**C-PSCēC- PIPēPrPē PIP·P°C”PjPsPrC-PN°.**

P»C-PeP°CḡCḡCHPeC- P·P°CḡPsP±Pē, CḡPeC- PIPīP»PēPIP°CḡC,CH PSP° PSC-PjPsPrPēPīC-PS

PḡC-PjPsPrPēPīC-PS PjPμC,P°P±PsP»C-P·CḡC”C,CHCḡCḡ C‡PμCḡPμP· CḡPēCḡC,PμPjCḡ  
C†PēC,PsC...CḡPsPjCḡ P450 3A4, P»PsPeP°P»C-P·PsPIP°PSCḡ CḡPe Cr CḡP»PēP·PsPIC-PN°  
PsP±PsP»PsPSC†C- PePēCēPμC‡PSPēPeCḡ, C,P°Pe C- PI PīPμC‡C-PSC†C-. PḡP°PePēPj C‡PēPSPsPj,

P»C-PeP°CḡCfCHbPeC- P·P°CfPsP±Pë, PIC-PrPsPjC- CḡPe C-PSPiC-P±C-C,PsCḡPë P°P±Ps C-PSPrCfPeC,PsCḡPë C†C-C”C— PμPSP·PëPjPSPsC— CḡPëCfC,PμPjPë, PiCḡPë PsPrPSPsC†P°CfPSPsPjCf P·P°CfC,PsCfCfPIP°PSPSC- PjPsPḡCfC,Ch PIPiP»PëPSCfC,Pë PSP° PiCḡPμCfPëCfC,PμPjPSPëPḡ PjPμC,P°P±PsP»C-P·Pj P°P±Ps PeP»C-CḡPμPSCf PSC-PjPsPrPëPiC-PSCf.

PμCḡPë P·P°CfC,PsCfCfPIP°PSPSC- PSC-PjPsPrPëPiC-PSCf PsPrPSPsC†P°CfPSPs P·PSPëPḡC†PμPSP°PIPμPrPμPSPëPjPë P»C-PeP°CḡCfCHbPePëPjPë P·P°CfPsP±P°PjPë CḡP»C-Pr PIP·CḡC,Pë PrPs CḡPIP°PiPë CḡC,CḡPiC-PSCH, P° C,P°PePsPḡ C,CḡPëPIP°P»C-CfC,Ch PIP·P°C”PjPsPrC-C—.

PḡPrPSPsC†P°CfPSPμ P·P°CfC,PsCfCfPIP°PSPSCḡ PSC-PjPsPrPëPiC-PSCf PiPμCḡPsCḡP°P»CHbPSPs C,P° CḡPëC,,P°PjPiC-C†PëPSCf P°P±Ps PiCḡPsC,PëPμPiC-P»PμPiC,PëC†PSPëC... P·P°CfPsP±C-PI, C%Ps C” C-PSPrCfPeC,PsCḡP°PjPë CḡPëCfC,PμPjPë C†PëC,PsC...CḡPsPjCf P450 3A4 (C,P°PeC- CḡPe C,,PμPSPsP±P°CḡP±C-C,P°P», C,,PμPSC-C,PsC—PS P°P±Ps PeP°CḡP±P°PjP°P·PμPiC-PS), PiCḡPsC,PëPiPsPeP°P·P°PSPμ. P·C,,PμPeC,PëPIPSC-CfC,Ch P»C-PeP°CḡCfCHbPePsPiPs P·P°CfPsP±Cḡ PḡC-C,PsPiC-PS PjPsPḡPμ P±CḡC,Pë P·PSPëPḡPμPSP°, CḡPeC%Ps PsPrPSPsC†P°CfPSPs P·P°CfC,PsCfPsPICḡCḡC,ChCḡCḡ C†C- P»C-PeP°CḡCfCHbPeC- P·P°CfPsP±Pë.

PḡPrPSPsC†P°CfPSPμ P·P°CfC,PsCfCfPIP°PSPSCḡ PiP°C†C-C”PSC,P°Pj P»C-C,PSCHbPsPiPs PIC-PeCḡ PSC-PjPsPrPëPiC-PSCf Cḡ PrPsP·C- 30 PjPi 3 CḡP°P·Pë PSP° PrPsP±Cḡ C,P° P°PSC,PëPrPμPiCḡPμCḡP°PSC,CḡPSPsCḡC,CḡPëPiC,PëP»C-PSCf PI PrPsP·C- 10 PjPi 3 CḡP°P·Pë PSP° PrPsP±Cḡ PiCḡPëP·PIPsPrPëP»Ps PrPs PSPμP·PSP°C†PSPsPiPs P·PSPëPḡPμPSPSCḡ PiP»P°P·PjPsPiPëC... CḡC-PIPSC-PI PSC-PjPsPrPëPiC-PSCf, C,PsPrC- CḡPe PiP»P°P·PjPsPIC- CḡC-PIPSC- PSPsCḡC,CḡPëPiC,PëP»C-PSCf PSPμ P·PjC-PSCHbPIP°P»PëCḡCḡ. P”PsP±PsPIP° PrPsP·P°, C%Ps P·P°CfC,PsCfPsPICḡC”C,ChCḡCḡ PiP°C†C-C”PSC,P°Pj C-P· CḡCḡP±P°CḡP°C...PSPsC—PrP°P»CHbPSPëPj PeCḡPsPIPsPiPëP»PëPiPsPj, Cḡ 4 CḡP°P·Pë PiPμCḡPμPiPëC%CḡC” PrPsP·Cḡ, C%Ps P·P°CfC,PsCfPsPICḡPIP°P»P°CḡCḡ Cḡ C†ChbPsPjCḡ PrPsCḡP»C-PrPḡPμPSPSC-, C,PsPjCḡ PeP»C-PSC-C†PSP° P·PSP°C†CḡC%C-CḡC,Ch C†C-C”C— PIP·P°C”PjPsPrC-C— PiCḡPë P»C-PeCḡPIP°PSPSC- CḡCḡP±P°CḡP°C...PSPsC—PrP°P»CHbPSPsPiPs PeCḡPsPIPsPiPëP»PëPiCḡ PIPSP°CḡP»C-PrPsPe CḡPsP·CḡPëPiCḡ P°PSPμPICḡPëP·PjPë PSPμ PiPëP·PSP°C†PμPSP°.

PμCḡPë PsPrPSPsC†P°CfPSPsPjCf P·P°CfC,PsCfCfPIP°PSPSC- P·PSP°CfC,CḡPiPSPëPjPë P»C-PeP°CḡCfCHbPePëPjPë P·P°CfPsP±P°PjPë, C%Ps C” C-PSPiC-P±C-C,PsCḡP°PjPë CḡPëCfC,PμPjPë C†PëC,PsC...CḡPsPjCf P450 3A4, CḡP»C-Pr PePsPSC,CḡPsP»CḡPIP°C,Pë P°CḡC,PμCḡC-P°P»CHbPSPëPḡ C,PëCḡPe C- Cḡ CḡP°P·C- PSPμPsP±C...C-PrPSPsCḡC,C- CḡPsP·PiP»CḡPSCfC,Pë PiPëC,P°PSPSCḡ PiCḡPs PePsCḡPëPiCḡPIP°PSPSCḡ PrPsP·Pë PSC-PjPsPrPëPiC-PSCf:

- PjP°PeCḡPsP»C-PrPSC- P°PSC,PëP±C-PsC,PëPePë (PSP°PiCḡPëPeP»P°Pr PμCḡPëC,CḡPsPjC-C†PëPS);

- PiCḡPsC,PëPIC-CḡCḡCḡPSC- P·P°CfPsP±Pë PrP»Cḡ P»C-PeCḡPIP°PSPSCḡ P’P†P>: C-PSPiC-P±C-C,PsCḡPë PiCḡPsC,PμP°P·Pë (PSP°PiCḡPëPeP»P°Pr CḡPëC,PsPSP°PIC-Cḡ);

- PiCḡPsC,PëPiCḡPëP±PePsPIC- P·P°CfPsP±Pë PiCḡCḡPiPë P°P·PsP»C-PI (PSP°PiCḡPëPeP»P°Pr PePμC,PsPePsPSP°P·PsP»);

- PSPμC,,P°P·PsPrPsPS.

PI<sup>o</sup>PsC<sup>+</sup>P<sup>o</sup> C,,PsC<sup>o</sup>PjP<sup>o</sup>P»CH<sup>o</sup>PsC- PrPsC<sup>o</sup>P»C-PrP<sup>o</sup>PI<sup>o</sup>PμPSPSC<sup>o</sup> PrP»C<sup>o</sup> PIP<sup>o</sup>PI<sup>o</sup>C<sup>+</sup>PμPSPSC<sup>o</sup> P<sup>o</sup>PsC,PμPSC<sup>+</sup>C-PN<sup>o</sup>PSPsC— PIP<sup>o</sup>·P<sup>o</sup>C<sup>o</sup>”PjPsPrC-C— PjC-P<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PSPsPj C,P<sup>o</sup> C<sup>+</sup>P<sup>o</sup>PjP<sup>o</sup> P»C-PeP<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>CT<sup>o</sup>CH<sup>o</sup>PeP<sup>o</sup>PjP<sup>o</sup> P·P<sup>o</sup>C<sup>o</sup>PsP±P<sup>o</sup>PjP<sup>o</sup> PSPμ P<sup>o</sup>CT<sup>o</sup>PsPIPsPrP<sup>o</sup>P»P<sup>o</sup>CT<sup>o</sup>C<sup>o</sup>, PSPμ PjPsP<sup>o</sup>PI<sup>o</sup>PSP<sup>o</sup> PIP<sup>o</sup>PeP»CT<sup>o</sup>C<sup>+</sup>P<sup>o</sup>C,P<sup>o</sup> PN<sup>o</sup>PjPsPIC-CT<sup>o</sup>PsC-CT<sup>o</sup>C,CH<sup>o</sup> P·P±C-P»CH<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> P<sup>o</sup>P»P<sup>o</sup>·PjPsPI<sup>o</sup>P<sup>o</sup>C... PePsPSC<sup>+</sup>PμPSC,CT<sup>o</sup>P<sup>o</sup>C<sup>+</sup>C-PN<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> (PrP<sup>o</sup>PI. CT<sup>o</sup>PsP·PrC-P» B«Ph<sup>o</sup>CT<sup>o</sup>PsP±P»P<sup>o</sup>PIPsCT<sup>o</sup>C,C- P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup>IB»).

P<sup>o</sup>hP·P<sup>o</sup>C,CT<sup>o</sup>PsPjC-C<sup>+</sup>P<sup>o</sup>PS C...PsC<sup>+</sup>P<sup>o</sup> C- PSP<sup>o</sup>P»PμP<sup>o</sup>PI<sup>o</sup>P<sup>o</sup>C,CH<sup>o</sup> P·P<sup>o</sup> CT<sup>o</sup>C,CT<sup>o</sup>C<sup>o</sup>PeC,C<sup>o</sup>CT<sup>o</sup>PsCT<sup>o</sup> PrPs PeP»P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup> PjP<sup>o</sup>PeCT<sup>o</sup>PsP»C-PrPSP<sup>o</sup>PeC... P<sup>o</sup>PSC,P<sup>o</sup>P±C-PsC,P<sup>o</sup>PeC-PI, PSPμ C<sup>o</sup> C-PSPI<sup>o</sup>C-P±C-C,PsCT<sup>o</sup>PsPj CYP3A4.

PhPrPSPsC<sup>+</sup>P<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPμ P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> P<sup>o</sup>P<sup>o</sup>C<sup>+</sup>C-C<sup>o</sup>PSC,P<sup>o</sup>Pj P»C-C,PSCH<sup>o</sup>PsPiPs PIC-PeC<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> C<sup>o</sup> PrPsP·C- 30 PjPi 2 CT<sup>o</sup>P<sup>o</sup>·P<sup>o</sup>P<sup>o</sup> PSP<sup>o</sup> PrPsP±C<sup>o</sup> C,P<sup>o</sup> P<sup>o</sup>PSC,P<sup>o</sup>PrPμP<sup>o</sup>CT<sup>o</sup>PμC<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup>,C<sup>o</sup> C,,P»C<sup>o</sup>PsPeCT<sup>o</sup>PμC,P<sup>o</sup>PSCT<sup>o</sup> 20 PjPi PSP<sup>o</sup> PrPsP±C<sup>o</sup> P<sup>o</sup>CT<sup>o</sup>P<sup>o</sup>·PIPsPrP<sup>o</sup>P»Ps PrPs P<sup>o</sup>CT<sup>o</sup>P<sup>o</sup>PI<sup>o</sup>P<sup>o</sup>C%PμPSPSC<sup>o</sup> CT<sup>o</sup>C-PI<sup>o</sup>PSC<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> C<sup>o</sup> P<sup>o</sup>P»P<sup>o</sup>·PjC- PeCT<sup>o</sup>PsPIC- PjP<sup>o</sup>PN<sup>o</sup>P<sup>o</sup>PI<sup>o</sup>Pμ PSP<sup>o</sup> 50 % C,P<sup>o</sup> P·PSP<sup>o</sup>C<sup>+</sup>PSPsPiPs P·PSP<sup>o</sup>P<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> CT<sup>o</sup>C-PI<sup>o</sup>PSC<sup>o</sup> C,,P»C<sup>o</sup>PsPeCT<sup>o</sup>PμC,P<sup>o</sup>PSCT<sup>o</sup> P±PμP· PIP<sup>o</sup>P»P<sup>o</sup>PI<sup>o</sup>C<sup>o</sup> PSP<sup>o</sup> PN<sup>o</sup>PsPiPs P<sup>o</sup>PeC,P<sup>o</sup>PI<sup>o</sup>PSP<sup>o</sup>PN<sup>o</sup> PjPμC,P<sup>o</sup>P±PsP»C-C, PSPsCT<sup>o</sup>C,,P»C<sup>o</sup>PsPeCT<sup>o</sup>PμC,P<sup>o</sup>PS (PrP<sup>o</sup>PI. CT<sup>o</sup>PsP·PrC-P» B«Ph<sup>o</sup>CT<sup>o</sup>PsP±P»P<sup>o</sup>PIPsCT<sup>o</sup>C,C- P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup>IB»).

PhPrPSPsC<sup>+</sup>P<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPμ P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> P· P<sup>o</sup>CT<sup>o</sup>PsC,P<sup>o</sup>CT<sup>o</sup>C<sup>o</sup>PrPsPjPSP<sup>o</sup>Pj P»C-PeP<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>CT<sup>o</sup>CH<sup>o</sup>PeP<sup>o</sup>Pj P·P<sup>o</sup>C<sup>o</sup>PsP±PsPj (PIP<sup>o</sup>P»CH<sup>o</sup>PiCT<sup>o</sup>PsC<sup>o</sup>PI<sup>o</sup> PeP<sup>o</sup>CT<sup>o</sup>P»PsC,P<sup>o</sup>) P<sup>o</sup>P±Ps P<sup>o</sup>PSC,P<sup>o</sup>PIPsPSC-CT<sup>o</sup>C,PsPj H<sub>2</sub>-CT<sup>o</sup>PμC<sup>+</sup>PμP<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C-PI (C<sup>+</sup>P<sup>o</sup>PjPμC,P<sup>o</sup>PrP<sup>o</sup>PS) PjPsP<sup>o</sup>PI<sup>o</sup>PμC<sup>o</sup>CT<sup>o</sup>C,P<sup>o</sup> PrPs P·P±C-P»CH<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> P<sup>o</sup>P»P<sup>o</sup>·PjPsPIPsC— PePsPSC<sup>+</sup>PμPSC,CT<sup>o</sup>P<sup>o</sup>C<sup>+</sup>C— PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> (PrP<sup>o</sup>PI. CT<sup>o</sup>PsP·PrC-P» B«Ph<sup>o</sup>CT<sup>o</sup>PsP±P»P<sup>o</sup>PIPsCT<sup>o</sup>C,C- P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup>IB»).

P—PIP<sup>o</sup>P<sup>o</sup>PI<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>P<sup>o</sup> PSP<sup>o</sup> PrPsCT<sup>o</sup>PI<sup>o</sup>C-Pr P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> P<sup>o</sup>PSC,P<sup>o</sup>PIPsPSC-CT<sup>o</sup>C,P<sup>o</sup> PeP<sup>o</sup>P»CH<sup>o</sup>C<sup>+</sup>C-CT<sup>o</sup> PSC-C,,PμPrP<sup>o</sup>PiC-PSC<sup>o</sup>, PsPrPSPsC<sup>+</sup>P<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPμ P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> P· C...C-PSC<sup>o</sup>PiCT<sup>o</sup>P<sup>o</sup>CT<sup>o</sup>C,P<sup>o</sup>PSPsPj/PrP<sup>o</sup>P»CH<sup>o</sup>C,,PsPiCT<sup>o</sup>P<sup>o</sup>CT<sup>o</sup>C,P<sup>o</sup>PSPsPj PjPsP<sup>o</sup>PI<sup>o</sup>Pμ P<sup>o</sup>CT<sup>o</sup>P<sup>o</sup>·PI<sup>o</sup>PμC<sup>o</sup>CT<sup>o</sup>C,P<sup>o</sup> PrPs P·P±C-P»CH<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> P<sup>o</sup>P»P<sup>o</sup>·PjPsPI<sup>o</sup>P<sup>o</sup>C... PePsPSC<sup>+</sup>PμPSC,CT<sup>o</sup>P<sup>o</sup>C<sup>+</sup>C-PN<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> (PrP<sup>o</sup>PI. CT<sup>o</sup>PsP·PrC-P» B«Ph<sup>o</sup>CT<sup>o</sup>PsP±P»P<sup>o</sup>PIPsCT<sup>o</sup>C,C- P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup>IB»).

P<sup>o</sup>PiP»P<sup>o</sup>PI PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> PSP<sup>o</sup> C-PSC<sup>o</sup>C- P»C-PeP<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>CT<sup>o</sup>CH<sup>o</sup>PeC- P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>PsP±P<sup>o</sup>

Pj PrPsCT<sup>o</sup>P»C-PrP<sup>o</sup>PI<sup>o</sup>PμPSPSC<sup>o</sup>C... PSP<sup>o</sup> C,PIP<sup>o</sup>C<sup>o</sup>P<sup>o</sup>PS<sup>o</sup>C... PIC<sup>o</sup>CT<sup>o</sup>C,P<sup>o</sup>PSPsPI<sup>o</sup>PμPSPs, C%Ps PsPrPSPsC<sup>+</sup>P<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPμ P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PSC<sup>o</sup> C,P<sup>o</sup> P·P<sup>o</sup>PrPsPIC<sup>o</sup>PrP<sup>o</sup>PSCT<sup>o</sup> P<sup>o</sup>CT<sup>o</sup>P<sup>o</sup>·PIPsPrP<sup>o</sup>C,CH<sup>o</sup> PrPs P·P±C-P»CH<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> AUC P·P<sup>o</sup>PrPsPIC<sup>o</sup>PrP<sup>o</sup>PSCT<sup>o</sup> C,P<sup>o</sup> P·PjPμPSC<sup>o</sup>PI<sup>o</sup>PSPSC<sup>o</sup> PN<sup>o</sup>PsPiPs PsP±P<sup>o</sup>CT<sup>o</sup>”PjC<sup>o</sup> CT<sup>o</sup>PsP·PiPsPrC-P»C<sup>o</sup> PN<sup>o</sup> PeP»C-CT<sup>o</sup>PμPSC<sup>o</sup>C<sup>o</sup>. P<sup>o</sup>hP»C-PSC-C<sup>+</sup>PSP<sup>o</sup> P·PSP<sup>o</sup>C<sup>+</sup>C<sup>o</sup>C%C-CT<sup>o</sup>C,CH<sup>o</sup> C<sup>+</sup>C-C”C— PIP<sup>o</sup>·P<sup>o</sup>C<sup>o</sup>”PjPsPrC-C— PSPμPIC-PrPsPjP<sup>o</sup>, P<sup>o</sup>P»Pμ, P·PIP<sup>o</sup>P<sup>o</sup>PI<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>P<sup>o</sup> PSP<sup>o</sup> PrPsP·PsP·P<sup>o</sup>P»PμP<sup>o</sup>PI<sup>o</sup>PSP<sup>o</sup>PN<sup>o</sup> C...P<sup>o</sup>CT<sup>o</sup>P<sup>o</sup>PeC,PμCT<sup>o</sup> P<sup>o</sup>CT<sup>o</sup>PsC,,C-P»CT<sup>o</sup> PiPsP±C-C<sup>+</sup>PSP<sup>o</sup>PeC... PμC,,PμPeC,C-PI P·P<sup>o</sup>PrPsPIC<sup>o</sup>PrP<sup>o</sup>PSCT<sup>o</sup>, C<sup>+</sup>CT<sup>o</sup> PIP<sup>o</sup>·P<sup>o</sup>C<sup>o</sup>”PjPsPrC-CT<sup>o</sup> C<sup>o</sup>P»C-Pr PIC<sup>o</sup>CT<sup>o</sup>P<sup>o</sup>C...PsPIC<sup>o</sup>PI<sup>o</sup>C,P<sup>o</sup> C<sup>o</sup> P<sup>o</sup>P<sup>o</sup>C<sup>+</sup>C-C”PSC,C-PI, C<sup>o</sup>PI<sup>o</sup>PeC- PsPrPSPsC<sup>+</sup>P<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPs PsC,CT<sup>o</sup>P<sup>o</sup>PjC<sup>o</sup>CT<sup>o</sup>C,CH<sup>o</sup> PSC-PjPsPrP<sup>o</sup>PiC-PS C,P<sup>o</sup> P·P<sup>o</sup>PrPsPIC<sup>o</sup>PrP<sup>o</sup>PS.

P<sup>+</sup>PSC<sup>o</sup>C- C,P<sup>o</sup>PiP<sup>o</sup> PIP<sup>o</sup>·P<sup>o</sup>C<sup>o</sup>”PjPsPrC-PN<sup>o</sup>

P”C-PiPsC,PμPSP·P<sup>o</sup>PI<sup>o</sup>PSC- P»C-PeP<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>CT<sup>o</sup>CH<sup>o</sup>PeC- P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>PsP±P<sup>o</sup>.

PμCT<sup>o</sup>P<sup>o</sup> PsPrPSPsC<sup>+</sup>P<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPsPjC<sup>o</sup> P·P<sup>o</sup>C<sup>o</sup>CT<sup>o</sup>C,PsCT<sup>o</sup>C<sup>o</sup>PI<sup>o</sup>PSPSC- PSC-PjPsPrP<sup>o</sup>PiC-PS PjPsP<sup>o</sup>PI<sup>o</sup>Pμ

PiPsCíPëP»CĤPIP°C,Pë PiC-PiPsC,PµPSP·PëPIPSPëPNë PµC,,PµPeC, C,P°PePëC...  
PiC-PiPsC,PµPSP·PëPIPSPëC... P»C-PeP°CĤCíCĤPePëC... P·P°CíPSP±C-PI:

- PrC-CíCĤPµC,PëPePë;
- P±PµC,P°-P±P»PsPeP°C,PsCĤPë;
- C-PSPiC-P±C-C,PsCĤPë PĥPµPα  
(P°PSPiC-PsC,PµPSP·PëPSPiPµCĤPµC,PIPsCĤCĤPIP°P»CĤPSPëPNë C,,PµCĤPjPµPSC,);
- A<sub>1</sub>-P°PSC,P°PiPsPSC-CíC,Pë;
- C-PSC€C- P°PSC,P°PiPsPSC-CíC,Pë PeP°P»CĤC†C-CĤ;
- P°P»CĤC,,P°-P°PrCĤPµPSPSP±P»PsPeP°C,PsCĤPë;
- C-PSPiC-P±C-C,PsCĤPë C,,PsCíC,,PsPrC-PµCíC,PµCĤP°P·Pë-5;
- P°P»CĤC,,P°-PjPµC,PëP»PrPsPiP°.

PĥPrPSP°Pe, CĤPeC%Ps PSPµPjPsP¶P»PëPIPs CíPSPëPePSCíC,Pë PePsPjP±C-PSP°C†C-PNë  
C,P°PePsPiPs C,PëPiCí, PSPµPsP±C...C-PrPSPs CíPIP°P¶PSPs CíC,PµP¶PëC,Pë P·P° CíC,P°PSPsPj  
PiP°C†C-C" PSC,P°.

PĥPµ CĤPµPePsPjPµPSPPrCíC"C,CĤCíCĤ PsPrPSPsC†P°CíPSPs P·PSC-PjPsPrPëPiC-PSPsPj  
PIP¶PëPIP°C,Pë PiCĤPµPNëPiC,,CĤCíC,PsPIPëPNë CíC-Pe, PsCíPeC-P»CĤPePë C†Pµ PjPsP¶Pµ  
PiCĤPëP·PIPµCíC,Pë PrPs P·P±C-P»CĤC€PµPSPSCĤ PiP»P°P·PjPsPIPëC...  
PePsPSC†PµPSC,CĤP°C†C-PNë PSC-PjPsPrPëPiC-PSCí C†PµCĤPµP· C-PSPiC-P±CíPIP°PSPSCĤ  
PsPePëCíPSPsPiPs PjPµC,P°P±PsP»C-P·PjCí PrPëPiC-PrCĤPsPiC-CĤPëPrPëPSC-PI. Pĥe  
PSP°CíP»C-PrPsPe, PjPsP¶Pµ PiPsCíPëP»CĤPIP°C,PëCíCĤ PiC-PiPsC,PµPSP·PëPIPSPëPNë  
PµC,,PµPeC,. PiPµPNë PµC,,PµPeC, PjPsP¶Pµ C,CĤPëPIP°C,Pë PiCĤPëPSP°PNëPjPSC- 4 PrPSC-  
PiC-CíP»CĤ PsCíC,P°PSPSCHPsPiPs PIP¶PëPIP°PSPSCĤ PiCĤPµPNëPiC,,CĤCíC,PsPIPsPiPs  
CíPsPeCí.

P"PsPIPµPrPµPSP° PIC-PrCíCíC,PSC-CíC,CĤ PIP·P°C"PjPsPrC-C—

Pj PrPsCíP»C-PrP¶PµPSPSC-, PI CĤPePsPjCí PIPëPIC†P°PICíCĤ PIPiP»PëPI  
P·P°CíC,PsCíCíPIP°PSPSCĤ 90 PjPi PSC-PjPsPrPëPiC-PSCí (Cí CĤPsP·PrC-P»PµPSPëC...  
PrPsP·P°C...) PiP°C†C-C" PSC,P°Pj P»C-C,PSCHPsPiPs PIC-PeCí, CĤPeC- PsC,CĤPëPjCíPIP°P»Pë  
PiP°P»PsPiPµCĤPëPrPsP», PSPµ PIPëCĤPIP»PµPSC- PsP·PSP°PePë PiPsC,PµPSC†C-PNëPSPëC...  
PIP·P°C"PjPsPrC-PNë. P—PSP°C†CíC%C-CíC,CĤ C†PëC... CĤPµP·CíP»CĤC,P°C,C-PI PrP»CĤ  
P·P°CíC,PsCíCíPIP°PSPSCĤ PiCĤPë CíCíP±P°CĤP°C...PSPsC—PrP°P»CĤPSPsPjCí  
PeCĤPsPIPsPIPëP»PëPIC- PSPµ PICíC,P°PSPsPIP»PµPSP°, PsCíPeC-P»CĤPePë PiCĤPë  
C†CĤPsPjCí PSC-PjPsPrPëPiC-PS P·P°CíC,PsCíPsPICíC"C,CĤCíCĤ Cí P±C-P»CĤC€  
PIPëCíPsPePëC... PrPsP·P°C....

PµCĤPë PsPrPSPsC†P°CíPSPsPjCí P·P°CíC,PsCíCíPIP°PSPSC- PSC-PjPsPrPëPiC-PSCí  
PiPµCĤPsCĤP°P»CĤPSPs C,P° PrC-P°P·PµPiP°PjCí, PrPëPiPsPeCíPëPSCí,  
PiP»C-P±PµPSPeP»P°PjC-PrCí, C-PSPrPsPjPµC,P°C†PëPSCí, CĤP°PSC-C,PëPrPëPSCí C,P°  
PIP°CĤC,,P°CĤPëPSCí PSPµ PIPëCĤPIPëP»Pë P¶PsPrPSPsC— PiPsC,PµPSC†C-PNëPSPsC—  
PIP·P°C"PjPsPrC-C—.

***PhCfPsp±P»PëPIPsCfC,C- P·P°CfC,PsCfCáPIP°PSPSCII.***

PkC-C,PsPiC-PS Cr C,,PsCfPjC- C,P°P±P»PµC,PsPe PSPµ CfP»C-Pr PsPrPSPsC±P°CfPSPs  
P·P°CfC,PsCfPSPICrPIP°C,Pë P· CfPSP·C±PëPSPsPj PSC-PjPsPrPëPiC-PSCr.

PkC-C,PsPiC-PS PSPµ CfP»C-Pr P·P°CfC,PsCfPSPICrPIP°C,Pë PiP°C†C-C"PSC,P°Pj C-P·  
CfCfP±P°CfP°C...PSPsC—PrP°P»CHPSPëPj PeCfPSPsPIPsPIPëP»PëPIPsPj PIPSP°CfP»C-PrPsPe  
C,CfP°PIPjPë, PsCfPeC-P»CHPePë PSPµ PICfC,P°PSPsPIP»PµPSPëPN  
CfPiCfPëCfC,P»PëPIPëPN PiCfPsC,,C-P»CH CfPiC-PIPIC-PrPSPsCëPµPSPSCII  
PePsCfPëCfC,CH/CfPëP·PëPe C,P° PrP»Cf C†CHPsPiPs PiPsPeP°P·P°PSPSCII PSPµ  
PjPsP¶CfC,CH P±CfC,Pë PIPëP·PSP°C±PµPSC- CfPiPµC†PëC,,C-C±PSC- PiCfCfPiPë  
PiP°C†C-C"PSC,C-PI, CfPeC- P± PsC,CfPëPjCfPIP°P»Pë PePsCfPëCfC,CH.

PkC-C,PsPiC-PS CfP»C-Pr P· PsP±PµCfPµP¶PSC-CfC,CH P·P°CfC,PsCfPSPICrPIP°C,Pë  
PiP°C†C-C"PSC,P°Pj C-P· PSP°P±CfCfPePsPj PjPsP·PeCf P°P±Ps PiC-PrPIPëC%PµPSPSCII  
PIPSCfC,CfC-CëPSCfPsC±PµCfPµPiPSPsPiPs C,PëCfPeCf C,CfP¶PePsPiPs CfC,CfPiPµPSCII.  
P¶PsC±P° PSPµ P±CfP»Ps PiCfPSPPrPµPjPsPSCfC,CfPSPIP°PSPs, C%Ps P»C-PeCfPIP°PSPSCII  
P»C-PeP°CfCfCHPePëPj P·P°CfPSP±PsPj PkC-C,PsPiC-PS P°CfPsC†C-CHC"C,CHCfCf P·  
PiC-PrPIPëC%PµPSPSCII Pj PIPSCfC,CfC-CëPSCfPsC±PµCfPµPiPSPsPiPs C,PëCfPeCf, Cr  
C,P°PePëC... PIPëPiP°PrPeP°C... P°P±Ps PiCfPë PiC-PrPIPëC%PµPSPSC- PIPjC-CfC,Cf PIPsPrPë  
Cf C,PeP°PSPëPSP°C... PjPsP·PeCf (PiPµPSPµCfP°P»C-P·PsPIP°PSPëPN PSP°P±CfCfPe  
PiPsP»PsPIPSPsPiPs PjPsP·PeCf) CfPµPePsPjPµPSPPrCfC"C,CHCfCf CfPµC,PµP»CHPSPëPN  
PePsPSC,CfPSP»CH CfC,P°PSCr PiP°C†C-C"PSC,P°.

PŸP»C-Pr PrPsC,CfPëPjCfPIP°C,PëCfCf PsP±PµCfPµP¶PSPsCfC,C- PiCfPë  
P»C-PeCfPIP°PSPSC- PiP°C†C-C"PSC,C-PI P· P°CfC,PµCfC-P°P»CHPSPsCH  
PiC-PiPsC,PµPSP·C-C"CH (CfPëCfC,PsP»C-C±PSPëPN C,PëCfPe PjPµPSCëPµ 100 PjPj CfC,,  
CfC,,).

Pj PiP°C†C-C"PSC,C-PI C-P· C†PëCfPSP·PsPj PiPµC±C-PSPePë, CfPeC- PsC,CfPëPjCfCfC,CH  
PkC-C,PsPiC-PS, PjPsP¶Pµ P·PSPëP¶CfPIP°C,PëCfCf PeP»C-CfPµPSCf  
P»C-PeP°CfCfCHPePsPiPs P·P°CfPSP±Cf, C,PsPjCf Cr C,P°PePëC... PiP°C†C-C"PSC,C-PI  
CfPµPePsPjPµPSPPrCfC"C,CHCfCf CfPµC,PµP»CHPSPëPN PePsPSC,CfPSP»CH  
P°CfC,PµCfC-P°P»CHPSPsPiPs C,PëCfPeCf.

PkC-PjPsPrPëPiC-PS PjPµC,P°P±PsP»C-P·CfC"C,CHCfCf PµPSP·PëPjPSPsCH  
CfPëCfC,PµPjPsCH C†PëC,PsC...CfPSPjCf P450 3A4. P»C-PeP°CfCfCHPeC- P·P°CfPSP±Pë,  
PIC-PrPsPjC- CfPe C-PSPiC-P±C-C,PsCfPë P°P±Ps C-PSPrCfPeC,PsCfPë C†C-C"C—  
PµPSP·PëPjPSPsC— CfPëCfC,PµPjPë, PjPsP¶CfC,CH PIPiP»PëPIP°C,Pë PSP°  
PiCfPµCfPëCfC,PµPjPSPëPN PjPµC,P°P±PsP»C-P·Pj P°P±Ps P·PjC-PSCHPIP°C,Pë  
PeP»C-CfPµPSCf PSC-PjPsPrPëPiC-PSCr (PrPëPI. CfPSP·PrC-P»Pë B«P·P·P°C"PjPsPrC-Cf P·  
C-PSCëPëPjPë P»C-PeP°CfCfCHPePëPjPë P·P°CfPSP±P°PjPë C,P° C-PSCëC- PIPëPrPë  
PIP·P°C"PjPsPrC-PNëB» C,P° B«PŸPiPsCfC-P± P·P°CfC,PsCfCfPIP°PSPSCII C,P° PrPsP·PëB» BŸ"  
B«PµP°C†C-C"PSC,Pë C-P· PiPsCfCfCëPµPSPSCII PjPë C,,CfPSPeC†C-C— PiPµC±C-PSPePëB»).

P"Ps P»C-PeP°CfCfCHPePëC... P·P°CfPSP±C-PI, PIC-PrPsPjPëC... CfPe C-PSPiC-P±C-C,PsCfPë  
PµPSP·PëPjCf C†PëC,PsC...CfPSPjCf P450 3A4 C- C%Ps PjPsP¶CfC,CH CfPiCfPëC±PëPSCfC,Pë  
P·P±C-P»CHCëPµPSPSCII PiP»P°P·PjPsPIPëC... PePsPSC†PµPSC,CfP°C†C-PN  
PSC-PjPsPrPëPiC-PSCr, PSP°P»PµP¶P°C,CH:

- PjP°PeCfPSP»C-PrPSC- P°PSC,PëP±C-PsC,PëPePë (PSP°PiCfPëPeP»P°Pr  
PµCfPëC,CfPSPjC-C†PëPS);

- $\text{PiC}\eta\text{PsC}, \text{P}\ddot{\text{e}}\text{PIC}-\text{C}\eta\text{C}\acute{\text{r}}\text{C}\acute{\text{r}}\text{PSC}-\text{P}\cdot\text{P}^{\circ}\text{C}\acute{\text{r}}\text{PsP}\pm\text{P}\ddot{\text{e}}\text{PrP}\gg\text{C}\eta\text{P}\gg\text{C}-\text{PeC}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\eta\text{P}\acute{\text{r}}\text{P}\ddot{\text{e}}\text{P}\text{:}$   
 $\text{C}-\text{PSPiC}-\text{P}\pm\text{C}-\text{C}, \text{PsC}\eta\text{P}\ddot{\text{e}}\text{PiC}\eta\text{PsC}, \text{P}\mu\text{P}^{\circ}\text{P}\cdot\text{P}\ddot{\text{e}}\text{ (PSP}^{\circ}\text{PiC}\eta\text{P}\ddot{\text{e}}\text{PeP}\gg\text{P}^{\circ}\text{Pr C}\eta\text{P}\ddot{\text{e}}\text{C}, \text{PsPSP}^{\circ}\text{PIC}-\text{C}\eta\text{)};$
- $\text{PiC}\eta\text{PsC}, \text{P}\ddot{\text{e}}\text{PiC}\eta\text{P}\ddot{\text{e}}\text{P}\pm\text{PePsPIC}-\text{P}\cdot\text{P}^{\circ}\text{C}\acute{\text{r}}\text{PsP}\pm\text{P}\ddot{\text{e}}\text{PiC}\eta\text{C}\acute{\text{r}}\text{P}\ddot{\text{e}}\text{P}^{\circ}\text{P}\cdot\text{PsP}\gg\text{C}-\text{PI}$   
 $(\text{PSP}^{\circ}\text{PiC}\eta\text{P}\ddot{\text{e}}\text{PeP}\gg\text{P}^{\circ}\text{Pr PeP}\mu\text{C}, \text{PsPePsPSP}^{\circ}\text{P}\cdot\text{PsP}\gg);$
- $\text{P}^{\circ}\text{PSC}, \text{P}\ddot{\text{e}}\text{PrP}\mu\text{PiC}\eta\text{P}\mu\text{C}\acute{\text{r}}\text{P}^{\circ}\text{PSC}, \text{P}\ddot{\text{e}}\text{PSP}\mu\text{C}, \text{P}^{\circ}\text{P}\cdot\text{PsPrPsPS C}-\text{C}, \text{P}\gg\text{C}\acute{\text{r}}\text{PsPeC}\acute{\text{r}}\text{P}\mu\text{C}, \text{P}\ddot{\text{e}}\text{PS};$
- $\text{C}\dots\text{C}-\text{PSC}\acute{\text{r}}\text{PiC}\eta\text{P}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{C}, \text{P}\ddot{\text{e}}\text{PS}/\text{PrP}^{\circ}\text{P}\gg\text{CHC}, \text{PsPiC}\eta\text{P}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{C}, \text{P}\ddot{\text{e}}\text{PS};$
- $\text{C}\ddot{\text{r}}\text{P}\ddot{\text{e}}\text{PjP}\mu\text{C}, \text{P}\ddot{\text{e}}\text{PrP}\ddot{\text{e}}\text{PS};$
- $\text{PIP}^{\circ}\text{P}\gg\text{CHPiC}\eta\text{PsC}^{\circ}\text{PIP}^{\circ}\text{PeP}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{P}\gg\text{PsC}, \text{P}^{\circ}.$

$\text{P}\mu\text{C}\eta\text{P}\ddot{\text{e}}\text{PsPrPSPsC}\ddot{\text{r}}\text{P}^{\circ}\text{C}\acute{\text{r}}\text{PSPsPjC}\acute{\text{r}}\text{P}\cdot\text{P}^{\circ}\text{C}\acute{\text{r}}\text{C}, \text{PsC}\acute{\text{r}}\text{C}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}-\text{P}\cdot\text{P}\pm\text{C}\acute{\text{r}}\text{PrCHC}-\text{C}\eta\text{PeP}\ddot{\text{e}}\text{Pj C}-\text{P}\cdot$   
 $\text{C}\ddot{\text{r}}\text{P}\ddot{\text{e}}\text{C}\dots\text{P}\gg\text{C}-\text{PeP}^{\circ}\text{C}\eta\text{C}\acute{\text{r}}\text{CHPeP}\ddot{\text{e}}\text{C}\dots\text{P}\cdot\text{P}^{\circ}\text{C}\acute{\text{r}}\text{PsP}\pm\text{C}-\text{PI C}\acute{\text{r}}\text{P}\gg\text{C}-\text{Pr PePsPSC}, \text{C}\eta\text{PsP}\gg\text{C}\eta\text{PIP}^{\circ}\text{C}, \text{P}\ddot{\text{e}}$   
 $\text{P}^{\circ}\text{C}\eta\text{C}, \text{P}\mu\text{C}\eta\text{C}-\text{P}^{\circ}\text{P}\gg\text{CHPSP}\ddot{\text{e}}\text{PN}\ddot{\text{e}}\text{C}, \text{P}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{Pe C}-\text{P}\cdot\text{P}^{\circ}\text{PSP}\mu\text{PsP}\pm\text{C}\dots\text{C}-\text{PrPSPsC}\acute{\text{r}}\text{C}, \text{C}-\text{P}\cdot\text{PSP}\ddot{\text{e}}\text{P}\cdot\text{P}\ddot{\text{e}}\text{C}, \text{P}\ddot{\text{e}}$   
 $\text{PrPsP}\cdot\text{C}\acute{\text{r}}\text{PSC}-\text{PjPsPrP}\ddot{\text{e}}\text{PiC}-\text{PSC}\acute{\text{r}}.$

$\text{P}-\text{P}^{\circ}\text{C}\acute{\text{r}}\text{C}, \text{PsC}\acute{\text{r}}\text{C}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\eta\text{C}\acute{\text{r}}\text{PiP}\mu\text{C}\eta\text{C}-\text{PsPr PIP}^{\circ}\text{PiC}-\text{C}, \text{PSPsC}\acute{\text{r}}\text{C}, \text{C}-\text{P}^{\circ}\text{P}\pm\text{Ps}$   
 $\text{PiPsPrC}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\eta\text{PiC}\eta\text{C}\acute{\text{r}}\text{PrPrCH}.$

$\text{P}^{\circ}\text{PiC}-\text{C}, \text{PSC}-\text{C}\acute{\text{r}}\text{C}, \text{CH}.$

$\text{P}^{\circ}\text{C}-\text{PrPiPsPIC}-\text{PrPSC}-\text{PePsPSC}, \text{C}\eta\text{PsP}\gg\text{CHPsPIP}^{\circ}\text{PSC}-\text{PrPsC}\acute{\text{r}}\text{P}\gg\text{C}-\text{PrP}\eta\text{P}\mu\text{PSPSC}\eta\text{C}\%_{\text{oo}}\text{PsPrPs}$   
 $\text{P}\cdot\text{P}^{\circ}\text{C}\acute{\text{r}}\text{C}, \text{PsC}\acute{\text{r}}\text{C}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\eta\text{P}\gg\text{C}-\text{PeP}^{\circ}\text{C}\eta\text{C}\acute{\text{r}}\text{CHPePsPiPs P}\cdot\text{P}^{\circ}\text{C}\acute{\text{r}}\text{PsP}\pm\text{C}\acute{\text{r}}\text{PIP}^{\circ}\text{PiC}-\text{C}, \text{PSP}\ddot{\text{e}}\text{Pj}$   
 $\text{P}\eta\text{C}-\text{PSPeP}^{\circ}\text{Pj PSP}\mu\text{PiC}\eta\text{PsIPsPrP}\ddot{\text{e}}\text{P}\gg\text{P}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{C}\eta. \text{P}^{\circ}\text{PsC}\acute{\text{r}}\text{P}\gg\text{C}-\text{PrP}\eta\text{P}\mu\text{PSPSC}\eta$   
 $\text{C}\eta\text{P}\mu\text{PiC}\eta\text{PsPrC}\acute{\text{r}}\text{PeC}, \text{P}\ddot{\text{e}}\text{PIPSPsC}-\text{C}, \text{PsPeC}\acute{\text{r}}\text{P}\ddot{\text{e}}\text{PePsP}\gg\text{PsPiC}-\text{C}-\text{PSP}^{\circ}\text{C}, \text{PIP}^{\circ}\text{C}\eta\text{P}\ddot{\text{e}}\text{PSP}^{\circ}\text{C}\dots\text{C}-\text{P}\cdot$   
 $\text{PiP}\mu\text{C}\eta\text{PsC}\eta\text{P}^{\circ}\text{P}\gg\text{CHPSP}\ddot{\text{e}}\text{Pj PIP}\mu\text{PrP}\mu\text{PSPSC}\eta\text{Pj PSC}-\text{PjPsPrP}\ddot{\text{e}}\text{PiC}-\text{PSC}\acute{\text{r}}$   
 $\text{PiC}\eta\text{PsPrP}\mu\text{PjPsPSC}\acute{\text{r}}\text{C}, \text{C}\eta\text{C}\acute{\text{r}}\text{PIP}^{\circ}\text{P}\gg\text{P}\ddot{\text{e}}\text{PIC}-\text{PrC}\acute{\text{r}}\text{C}\acute{\text{r}}\text{C}, \text{PSC}-\text{C}\acute{\text{r}}\text{C}, \text{CH C}, \text{P}\mu\text{C}\eta\text{P}^{\circ}\text{C}, \text{PsPiP}\mu\text{PSPSPsPiPs}$   
 $\text{PIP}\ddot{\text{e}}\text{P}\gg\text{P}\ddot{\text{e}}\text{PIC}\acute{\text{r}}, \text{PsPrPSP}^{\circ}\text{Pe C}\acute{\text{r}}\text{PrPsC}\acute{\text{r}}\text{P}\gg\text{C}-\text{PrP}\eta\text{P}\mu\text{PSPSC}\eta\text{C}\dots\text{PSP}^{\circ}\text{C}, \text{PIP}^{\circ}\text{C}\eta\text{P}\ddot{\text{e}}\text{PSP}^{\circ}\text{C}\dots$   
 $\text{PiC}\eta\text{PsPrP}\mu\text{PjPsPSC}\acute{\text{r}}\text{C}, \text{C}\eta\text{PsPIP}^{\circ}\text{PSP}^{\circ}\text{C}\eta\text{P}\mu\text{PiC}\eta\text{PsPrC}\acute{\text{r}}\text{PeC}, \text{P}\ddot{\text{e}}\text{PIPSP}^{\circ}\text{C}, \text{PsPeC}\acute{\text{r}}\text{P}\ddot{\text{e}}\text{C}\ddot{\text{r}}\text{PSC}-\text{C}\acute{\text{r}}\text{C}, \text{CH}.$   
 $\text{P}\ddot{\text{e}}\text{PeC}\%_{\text{oo}}\text{Ps PSC}-\text{PjPsPrP}\ddot{\text{e}}\text{PiC}-\text{PS PSP}\mu\text{PsP}\pm\text{C}\dots\text{C}-\text{PrPSPs P}\cdot\text{P}^{\circ}\text{C}\acute{\text{r}}\text{C}, \text{PsC}\acute{\text{r}}\text{PsPIC}\acute{\text{r}}\text{PIP}^{\circ}\text{C}, \text{P}\ddot{\text{e}}\text{PiC}-\text{Pr}$   
 $\text{C}\ddot{\text{r}}\text{P}^{\circ}\text{C}\acute{\text{r}}\text{PIP}^{\circ}\text{PiC}-\text{C}, \text{PSPsC}\acute{\text{r}}\text{C}, \text{C}-, \text{C}\acute{\text{r}}\text{P}\gg\text{C}-\text{Pr C}\eta\text{P}\mu\text{C}, \text{P}\mu\text{P}\gg\text{CHPSPs P}\cdot\text{PIP}^{\circ}\text{P}\eta\text{P}\ddot{\text{e}}\text{C}, \text{P}\ddot{\text{e}}$   
 $\text{PePsC}\eta\text{P}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{C}, \text{CH C}, \text{P}^{\circ}\text{PiPsC}, \text{P}\mu\text{PSC}\ddot{\text{r}}\text{C}-\text{PN}\ddot{\text{e}}\text{PSC}-\text{C}\eta\text{P}\ddot{\text{e}}\text{P}\cdot\text{P}\ddot{\text{e}}\text{PeP}\ddot{\text{e}}\text{P}\cdot\text{P}^{\circ}\text{P}\gg\text{P}\mu\text{P}\eta\text{PSPs PIC}-\text{Pr}$   
 $\text{C}, \text{C}\eta\text{P}\eta\text{PePsC}\acute{\text{r}}\text{C}, \text{C}-\text{PeP}\gg\text{C}-\text{PSC}-\text{C}\ddot{\text{r}}\text{PSPsC}-\text{PeP}^{\circ}\text{C}\eta\text{C}, \text{P}\ddot{\text{e}}\text{PSP}\ddot{\text{e}}.$

$\text{P}\mu\text{P}\mu\text{C}\eta\text{C}-\text{PsPr PiPsPrC}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\eta\text{PiC}\eta\text{C}\acute{\text{r}}\text{PrPrCH}.$

$\text{P}\ddot{\text{e}}\text{C}\eta\text{PIP}\gg\text{P}\mu\text{PSPs}, \text{C}\%_{\text{oo}}\text{Ps PePsPSC}\ddot{\text{r}}\text{P}\mu\text{PSC}, \text{C}\eta\text{P}^{\circ}\text{C}\ddot{\text{r}}\text{C}-\text{C}\eta\text{PSC}-\text{PjPsPrP}\ddot{\text{e}}\text{PiC}-\text{PSC}\acute{\text{r}}\text{C}, \text{P}^{\circ}\text{PN}\ddot{\text{e}}\text{PsPiPs}$   
 $\text{PjP}\mu\text{C}, \text{P}^{\circ}\text{P}\pm\text{PsP}\gg\text{C}-\text{C}, \text{C}-\text{PI C}\acute{\text{r}}\text{PiC}\eta\text{C}\acute{\text{r}}\text{PrPSPsPjC}\acute{\text{r}}\text{PjPsP}\gg\text{PsC}\ddot{\text{r}}\text{C}-\text{P}\cdot\text{P}^{\circ}\text{PiPsC}\eta\text{C}\eta\text{PrPePsPj}$   
 $\text{PIP}\mu\text{P}\gg\text{P}\ddot{\text{e}}\text{C}\ddot{\text{r}}\text{P}\ddot{\text{e}}\text{PS PIC}-\text{PrPiPsPIC}-\text{PrP}^{\circ}\text{C}^{\circ}\text{PePsPSC}\ddot{\text{r}}\text{P}\mu\text{PSC}, \text{C}\eta\text{P}^{\circ}\text{C}\ddot{\text{r}}\text{C}-\text{C}-\text{C}\acute{\text{r}}\text{PiP}\gg\text{P}^{\circ}\text{P}\cdot\text{PjC}-$   
 $\text{PeC}\eta\text{PsPIC}-\text{PjP}^{\circ}\text{C}, \text{P}\mu\text{C}\eta\text{C}-, \text{P}\mu\text{C}-\text{Pr C}\ddot{\text{r}}\text{P}^{\circ}\text{C}\acute{\text{r}}\text{C}, \text{PsC}\acute{\text{r}}\text{C}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\eta\text{PSC}-\text{PjPsPrP}\ddot{\text{e}}\text{PiC}-\text{PSC}\acute{\text{r}}$   
 $\text{C}\acute{\text{r}}\text{P}\gg\text{C}-\text{Pr PiC}\eta\text{P}\ddot{\text{e}}\text{PiP}\ddot{\text{e}}\text{PSP}\ddot{\text{e}}\text{C}, \text{P}\ddot{\text{e}}\text{PiPsPrC}\acute{\text{r}}\text{PIP}^{\circ}\text{PSPSC}\eta\text{PiC}\eta\text{C}\acute{\text{r}}\text{PrPrCH}.$

$\text{P P}\mu\text{PiC}\eta\text{PsPrC}\acute{\text{r}}\text{PeC}, \text{P}\ddot{\text{e}}\text{PIPSP}^{\circ}\text{C}, \text{C}\acute{\text{r}}\text{PSPeC}\ddot{\text{r}}\text{C}-\text{C}\eta.$

$\text{Pj PiPsPsPrP}\ddot{\text{e}}\text{PSPsPeP}\ddot{\text{e}}\text{C}\dots\text{PIP}\ddot{\text{e}}\text{PiP}^{\circ}\text{PrPeP}^{\circ}\text{C}\dots\text{PI C}\acute{\text{r}}\text{PjPsPIP}^{\circ}\text{C}\dots\text{P}\cdot\text{P}^{\circ}\text{PiP}\gg\text{C}-\text{PrPSP}\mu\text{PSPSC}\eta\text{in}$   
 $\text{vitro P}^{\circ}\text{PSC}, \text{P}^{\circ}\text{PiPsPSC}-\text{C}\acute{\text{r}}\text{C}, \text{P}\ddot{\text{e}}\text{PeP}^{\circ}\text{P}\gg\text{CHC}\ddot{\text{r}}\text{C}-\text{CH P}^{\circ}\text{C}\acute{\text{r}}\text{PsC}\ddot{\text{r}}\text{C}-\text{CHPIP}^{\circ}\text{P}\gg\text{P}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{C}\eta\text{P}\cdot$   
 $\text{PsP}\pm\text{PsC}\eta\text{PsC}, \text{PSP}\ddot{\text{e}}\text{PjP}\ddot{\text{e}}\text{P}\pm\text{C}-\text{PsC}\dots\text{C}-\text{PjC}-\text{C}\ddot{\text{r}}\text{PSP}\ddot{\text{e}}\text{PjP}\ddot{\text{e}}\text{P}\cdot\text{PjC}-\text{PSP}^{\circ}\text{PjP}\ddot{\text{e}}\text{PI PrC}-\text{P}\gg\text{C}\eta\text{PSC}\ddot{\text{r}}\text{C}-$   
 $\text{PiPsP}\gg\text{C}-\text{PIPeP}\ddot{\text{e}}\text{C}\acute{\text{r}}\text{PiP}\mu\text{C}\eta\text{PjP}^{\circ}\text{C}, \text{PsP}\cdot\text{PsC}-\text{PrC}-\text{PI}, \text{C}\%_{\text{oo}}\text{Ps PjPsP}\eta\text{P}\mu\text{PiC}\eta\text{P}\ddot{\text{e}}\text{P}\cdot\text{PiPsPrP}\ddot{\text{e}}\text{C}, \text{P}\ddot{\text{e}}\text{PrPs}$

PiPsC<sub>7</sub>CrCePμPSPSCII C,,CíPSPeC†C-C— Cl'PiPμC<sub>7</sub>PjPë. PkPμPIC-PrPsPjPs,  
PSP°Cl'PeC-P»CHbPePë P·PSP°C‡CrC%oPëPjPë C'' C†C- P·PjC-PSPë PiC<sub>7</sub>Pë  
PePsC<sub>7</sub>PsC,PePsC,C<sub>7</sub>PëPIP°P»PsPjCr P»C-PeCíPIP°PSPSC-.

$P-PrP^oC, PSC-ClC, CH_2PIP \gg P\ddot{e}PIP^oC, P\ddot{e}PSP^oC \in PIP\ddot{e}PrPeC-ClC, CH_2C_7P_{\mu}P^oPeC \dagger C-C-P\ddot{i}C_7P\ddot{e}PeP_{\mu}C_7C \hat{z} PIP^oPSPSC-P^oPIC, PsC, C_7P^oPSC \ddot{I}P\ddot{i}PsC_7C, PsPjP^oP \pm PsC-PSC \in P\ddot{e}PjP\ddot{e}PjP_{\mu}C \dots P^oPSC-P-PjP^oPjP\ddot{e}.$

P—PrP°C, PSC—CfC, CH PiP°C†C—C" PSC, P° PePμCfCfPPIP°C, Pë P°PIC, PsC, CfP°PSCfPiPsCfC, PsPj P°P±Ps PiCfP°C†CfPPIP°C, Pë P· C—PSC€PëPjPë PjPμC...P°PSC—P·PjP°PjPë PjPsP¶Pμ P±CfC, Pë PiPsCfCfC€PμPSP° Cf P·PIBf™C¶P·PeCf P· PjPsP¶P»PëPIPëPj PIPëPSPëPePSPμPSPSC¶Pj P·P°PiP°PjPsCfPsC‡PμPSPSC¶.

***PŸPİPsCÍĆ-P± P·P°CÍĆ,PsCÍĆ¿PIP°PSPSCİ C,P° PŕPsP·Pë.***

$P\check{Y}C\acute{a}P\pm P^{\circ}C\check{H}P^{\circ}C\dots PSPsC-P\tau P^{\circ}P\gg CH\check{b}PSP\check{e}P\check{N}\check{e}P\check{e}C\check{H}PsPIP\check{s}PIP\check{e}P\gg P\check{e}PIPIPSP^{\circ}C\acute{I}P\gg C-P\tau PsPe$   
 $C\check{H}PsP\cdot C\check{H}P\check{e}PIC\acute{a}P^{\circ}PSP\mu PIC\check{H}P\check{e}P\cdot PjP\check{e}$

P PμPePsPjPμPSPrPsPIP°PSP° PrPsP·P° CΓC,P°PSPsPIPëC,CH<sub>2</sub>C,P°P±P»PμC,PePë.  
 PμCηPëPNëPjP°CηC,CH<sub>2</sub>P·C-PSC,PμCηPIP°P»P°PjPë 4 PiPsPrPëPSPë (P·P°PiP°P»CH<sub>2</sub>PSP°  
 PrPsP±PsPIP° PrPsP·P° вЂ“ 360 PjPi), P·P°PiPëPIP°CηC±Pë PIPsPrPsCη.  
 P—P°CΓC,PsCΓCΓPIP°PSPSCΠ CΓP»C-Pr CηPsP·PiPsC±P°C,Pë PIPiCηPsPrPsPIP¶ 4 PrPSC-Pi  
 PiC-CΓP»CΠ CΓCΓP±P°CηP°C...PSPSc—PrP°P»CH<sub>2</sub>PSPsPiPs PeCηPsPIPsPIPëP»PëPICΓ,  
 C,CηPëPIP°P»C-CΓC,CH<sub>2</sub>PiCηPëPNëPsPjCΓ вЂ“ 21 PrPμPSCη.

Pj C<sub>7</sub>P<sup>o</sup>·C- PiC<sub>7</sub>PsPIPμP<sub>7</sub>PμPSPSC<sub>7</sub> PsPiPμC<sub>7</sub>P<sup>o</sup>C, PēPIPSPsPiPs PIC, C<sub>7</sub>CrC<sub>7</sub>P<sup>o</sup>PSPSC<sub>7</sub> P·P<sup>o</sup>C<sub>7</sub>C, PsC<sub>7</sub>CrPIP<sup>o</sup>PSPSC<sub>7</sub> P»C- PeP<sup>o</sup>C<sub>7</sub>C<sub>7</sub>CH<sub>7</sub>PePsPiPs P·P<sup>o</sup>C<sub>7</sub>PsP±Cr P<sub>7</sub>C-C, PsPiC-PS C<sub>7</sub>P»C-Pr PiC<sub>7</sub>PsPrPsPIP¶PēC, Pē (Cr P·P<sup>o</sup>·PSP<sup>o</sup>C<sub>7</sub>PμPSPsPjCr PIPēC%<sub>o</sub>Pμ PrPsP·CrPIP<sup>o</sup>PSPSC-) PrPs P·P<sup>o</sup>PIPμC<sub>7</sub>C€PμPSPSC<sub>7</sub> 21-PrPμPSPSPsPiPs PiPμC<sub>7</sub>C-PsPrCr P»C- PeCrPIP<sup>o</sup>PSPSC<sub>7</sub>.

PJ C<sub>7</sub>H<sub>9</sub>P<sup>o</sup>·C- C<sub>7</sub>H<sub>9</sub>PsP·PIPëC,PeC<sub>7</sub> P<sub>i</sub>PsP±C-C±PSPëC... C<sub>7</sub>H<sub>9</sub>µP<sup>o</sup>PeC†C-PM<sub>9</sub> P·P<sup>o</sup> P<sub>i</sub>PsC,C<sub>7</sub>H<sub>9</sub>µP±Pë C†P»C-Pr P·PjµPSPC€PëC,Pë PrPsP·C<sub>7</sub> P<sup>o</sup>P±Ps P<sub>i</sub>C<sub>7</sub>H<sub>9</sub>PëP<sub>i</sub>PëPSPëC,Pë P»C-PeC<sub>7</sub>PIP<sup>o</sup>PSPSC¶.

$P\check{Y}C\acute{a}P_{\pm}P^{\circ}C\check{H}P^{\circ}C...PSPsC-PrP^{\circ}P\rangle CHbPSP\ddot{e}Pn\text{ }PeC\check{H}PsPIP_sPIP\ddot{e}P\rangle P\ddot{e}PI\text{ }PIPSP^{\circ}C\acute{I}P\rangle C-PrPsPe$   
 $C,C\check{H}P^{\circ}PIP_jP\ddot{e}$

P—P°CÍC,PsCÍCíPIP°PSPSCЦ PSC—PjPsPrPëPíC—PSCí PSPµ CĤPµPePsPjPµPSPPrCíC”C,CHCÍCЦ,  
PsCÍCPeC—P»CHPePë PSPµ PICÍC,P°PSPsPIP»PµPSPëPñ CÍPíCĤPëCЦC,P»PëPIPëPñ  
PiCĤPsC,,C—P»CH PePsCĤPëCÍC,CH/CĤPëP·PëPe.

$$P\mu^{\circ}C\uparrow C-C''PSC,P\ddot{e} P\cdot P\ddot{i}PsC\overline{H}C\acute{z}C\epsilon P\mu PSPSC\downarrow PjP\ddot{e} C,,C\acute{z}PSPeC\uparrow C-C-P\ddot{i}P\mu C\ddagger C-PSPeP\ddot{e}$$

$\text{P}_{\mu}\text{C}\overline{\text{H}}\text{P}\ddot{\text{e}}\text{C}, \text{C}\overline{\text{I}}\text{P}\overline{\text{I}}\text{P}\text{ePsPjCr}\text{P}\ddot{\text{I}}\text{PsC}\overline{\text{H}}\text{CrC}\overline{\text{e}}\text{P}_{\mu}\text{PSPSC}-\text{C}, \text{CrPSPeC}\overline{\text{I}}\text{C}-\text{C}-\text{P}\ddot{\text{I}}\text{P}_{\mu}\text{C}\overline{\text{I}}\text{C}-\text{PSPeP}\ddot{\text{e}},$   
 $\text{P}\cdot\text{PsPeC}\overline{\text{H}}\text{P}_{\mu}\text{PjP}^{\circ}\text{P}\ddot{\text{I}}\text{C}\overline{\text{H}}\text{P}\ddot{\text{e}}\text{C}\overline{\text{I}}\text{P}\text{PsP}\cdot\text{C}-\text{P}\ddot{\text{I}}\text{P}_{\mu}\text{C}\overline{\text{I}}\text{C}-\text{PSPeP}\ddot{\text{e}}, \text{P}\pm\text{C}-\text{PsPrPsC}\overline{\text{I}}\text{C}, \text{CrP}\ddot{\text{I}}\text{PSC}-\text{C}\overline{\text{I}}\text{C}, \text{CH}$   
 $\text{PSC}-\text{PjPsPrP}\ddot{\text{e}}\text{P}\ddot{\text{I}}\text{C}-\text{PSCr}\text{PjPsP}\overline{\text{I}}\text{P}_{\mu}\text{P}\cdot\text{P}\pm\text{C}-\text{P}\gg\text{CHC}\overline{\text{e}}\text{CrPIP}^{\circ}\text{C}, \text{P}\ddot{\text{e}}\text{C}\overline{\text{I}}\text{C}\overline{\text{I}}\text{PIPSP}^{\circ}\text{C}\overline{\text{I}}\text{P}\gg\text{C}-\text{PrPsPe}$   
 $\text{P}\cdot\text{PSP}\ddot{\text{e}}\text{P}\overline{\text{I}}\text{P}_{\mu}\text{PSPSC}\overline{\text{I}}\text{P}\ddot{\text{I}}\text{C}\overline{\text{H}}\text{P}_{\mu}\text{C}\overline{\text{I}}\text{P}\ddot{\text{e}}\text{C}\overline{\text{I}}\text{C}, \text{P}_{\mu}\text{PjPSPsPiPsPjP}_{\mu}\text{C}, \text{P}^{\circ}\text{P}\pm\text{PsP}\gg\text{C}-\text{P}\cdot\text{PjCr}\text{C}, \text{P}^{\circ}$   
 $\text{PjP}_{\mu}\text{C}, \text{P}^{\circ}\text{P}\pm\text{PsP}\gg\text{C}-\text{C}\overline{\text{I}}\text{PSPsPiPsPeP}\gg\text{C}-\text{C}\overline{\text{H}}\text{P}_{\mu}\text{PSC}\overline{\text{I}}\text{Cr}. \text{P}''\text{C}-\text{C}\overline{\text{I}}\text{P}\gg\text{C}-\text{PeP}^{\circ}\text{C}\overline{\text{H}}\text{C}\overline{\text{I}}\text{CHPePsPiPs}$   
 $\text{P}\cdot\text{P}^{\circ}\text{C}\overline{\text{I}}\text{PsP}\pm\text{Cr}\text{C}, \text{P}^{\circ}\text{P}\ddot{\text{I}}\text{PsP}\pm\text{C}-\text{C}\overline{\text{I}}\text{PSC}-\text{C}\overline{\text{H}}\text{P}_{\mu}\text{P}^{\circ}\text{PeC}\overline{\text{I}}\text{C}-\text{C}-, \text{PSP}^{\circ}\text{P}\ddot{\text{I}}\text{C}\overline{\text{H}}\text{P}\ddot{\text{e}}\text{PeP}\gg\text{P}^{\circ}\text{Pr}$   
 $\text{P}\cdot\text{PSP}\ddot{\text{e}}\text{P}\overline{\text{I}}\text{P}_{\mu}\text{PSPSC}\overline{\text{I}}\text{P}^{\circ}\text{C}\overline{\text{H}}\text{C}, \text{P}_{\mu}\text{C}\overline{\text{H}}\text{C}-\text{P}^{\circ}\text{P}\gg\text{CHPSPsPiPsC}, \text{P}\ddot{\text{e}}\text{C}\overline{\text{I}}\text{PeCr}, \text{Cr}\text{C}\overline{\text{I}}\text{P}\ddot{\text{e}}\text{C}...$

PIP°C†C-C" PSC,C-PI PjPsP¶C†C,CH P±C†C,Pë P±C-P»CHC€ PIPëC¶P°P¶PµPSPëPjPë.

PJ C,P°PePëC... PIPëPIP°PrPeP°C... PrPsP·C† C†P»C-Pr P·PjPµPSC€PëC,Pë (P·P°P»PµP¶PSPs PIC-Pr P°C¶C,PµC¶C-P°P»CHBSPSPiPs C,PëC†PeC†), P° C† C¶P°P·C- PSPµPsP±C...C-PrPSPsC†C,C- B¶" P†C¶PëPIPëPSPëC,Pë P»C-PeC†PIP°PSPSC¶.

PµC¶Pë PsPrPSPsC†P°C†PSPsPjC† P·P°C†C,PsC†C†PIP°PSPSC- P· C-PSPiC-P±C-C,PsC¶P°PjPë P°P±Ps C-PSP†C†PeC,PsC¶P°PjPë CYP 3A4 PjPsP¶Pµ PIPëPSPëPePSC†C,Pë P†PsC,C¶PµP±P° C† PePsC¶PµPeC†C-C— PrPsP·Pë (PrPëPI. C¶PsP·PrC-P» B«P'P·P°C" PjPsPrC-C¶ P· C-PSC€PëPjPë P»C-PeP°C¶C†CHPePëPjPë P·P°C†PsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNëB»).

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

PkC†PsP±P»PëPIC- PIPëPjPsPiPë C%PsPrPs PrPsP·C†PIP°PSPSC¶ P†C¶Pë P·P°C†C,PsC†C†PIP°PSPSC- P†P°C†C-C" PSC,P°Pj P»C-C,PSCHBPsPiPs PIC-PeC† PIC-PrC†C†C,PSC-.

PŸP†PsC†C-P± P·P°C†C,PsC†C†PIP°PSPSC¶

PŸP°P±P»PµC,PePë C†P»C-Pr PePsPIC,P°C,Pë C†C-P»PëPjPë, P·P°P†PëPIP°C¶C†Pë PSPµPIPµP»PëPePsC¶ PeC-P»CHPeC-C†C,C¶ C¶C-PrPëPSPë, PSPµP·P°P»PµP¶PSPs PIC-Pr P†C¶PëPNëPsPjC† C—P¶C-. P†PSC,PµC¶PIP°P» PjC-P¶ P†PsC†P»C-PrPsPIPSPëPjPë PrPsP·P°PjPë P†PsPIPëPSPµPS C†C,P°PSPsPIPëC,Pë PSPµ PjPµPSC€Pµ 4 P†PsPrPëPS.

PkPµPsP±C...C-PrPSPs C†PSPëPeP°C,Pë PIP¶PëPIP°PSPSC¶ P†C¶PµPNëP†C,,C¶C†C,PsPIPSPiPs C†PsPeC† (PrPëPI. C¶PsP·PrC-P» B«P'P·P°C" PjPsPrC-C¶ P· C-PSC€PëPjPë P»C-PeP°C¶C†CHPePëPjPë P·P°C†PsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNëB»).

*P" C-C,Pë.*

P'PµP·P†PµPeP° C,P° PµC,,PµPeC,PëPIPSC-C†C,CH P·P°C†C,PsC†C†PIP°PSPSC¶ PSC-PjPsPrPëP†C-PSC† P†P°C†C-C" PSC,P°Pj PIC-PePsPj PrPs 18 C¶PsPeC-PI PSPµ PIC†C,P°PSPsPIP»PµPSC-.

P»C-PeP°C¶C†CHPePëPNë P·P°C†C-P± PSPµ P·P°C†C,PsC†PsPIC†C¶C,CH PrC-C,C¶Pj.

***PµPµC¶PµPrPsP·CžPIP°PSPSC¶.***

*PŸPëPjP†C,PsPjPë.* PµC¶Pë P†PsC†C,C¶PsPjC† P†PµC¶PµPrPsP·C†PIP°PSPSC- C†P†PsC†C,PµC¶C-P†P°C¶C,CHC†C¶ PIPëC¶P°P¶PµPSP° P°C¶C,PµC¶C-P°P»CHBSPSP° P†C-P†PsC,PµPSP·C-C¶, C,P°C...C-PeP°C¶PrC-C¶ P°P±Ps P±C¶P°PrPëPeP°C¶PrC-C¶, P° C† C¶P°P·C- P†PµC¶PsC¶P°P»CHBSPSPiPs P·P°C†C,PsC†C†PIP°PSPSC¶ B¶" C¶PsP·P»P°PrPë P· P±PsPeC† C€P»C†PSPePsPIPs-PePëC€PePsPIPsPiPs C,C¶P°PeC,C† C,P° PSC†PrPsC,P°.

*P»C-PeCžPIP°PSPSC¶.* PµC¶Pë P†PsC†C,C¶PsPjC† P†PµC¶PµPrPsP·C†PIP°PSPSC- PSPµPsP±C...C-PrPSPs PSPµP†P°PNëPSPs P†C¶PëPIPëPSPëC,Pë P·P°C†C,PsC†C†PIP°PSPSC¶ P†C¶PµP†P°C¶P°C,C† PkC-C,PsP†C-PS. PµC¶Pë P†C¶PëP·PSP°C†PµPSPSC- PµPeC†C,C¶PµPSPsC— PrPsP†PsPjPsPiPë P†PsPeP°P·P°PSP° C†PëPjP†C,PsPjP°C,PëC†PSP° C,PµC¶P°P†C-C¶. PµC¶Pë P†PµC¶PsC¶P°P»CHBSPSPjC† P·P°C†C,PsC†C†PIP°PSPSC- PSC-PjPsPrPëP†C-PSC† C¶Pe

$P \cdot P^{\circ} C \dots C - Pr$   $P_{\mu}PeC\acute{I}C, C\grave{H}P_{\mu}PSPsC - C, P_{\mu}C\grave{H}P^{\circ}P\acute{I}C - C - C\grave{H}P_{\mu}PePsPjP_{\mu}PSPPrC\acute{r}C''C, CHC\acute{I}C\grave{I}$   
 $P\acute{I}C\grave{H}PsPjP\ddot{e}PIP^{\circ}PSPSC\grave{I} C\acute{E}P \gg C\acute{r}PSPeP^{\circ} P \cdot P\acute{I}PsPrP^{\circ}P \gg CHC\acute{E}P\ddot{e}Pj P \cdot P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC\grave{I}Pj$   
 $P^{\circ}PeC, P\ddot{e}IPsPIP^{\circ}PSPsPiPs PIC\acute{r}PiC - P \gg P \gg C\grave{I}. P_{\mu}C\grave{H}P\ddot{e} C\acute{I}C\acute{r}C, C, C''PIP sPjC\acute{r} P \cdot PSP\ddot{e}P\grave{I}P_{\mu}PSPSC -$   
 $P^{\circ}C\grave{H}C, P_{\mu}C\grave{H}C - P^{\circ}P \gg CH\ddot{H}PSPsPiPs C, P\ddot{e}C\acute{I}P\acute{e}C\acute{r} PIPSC\acute{r}C, C\grave{H}C - C\acute{E}PSC\ddot{H}PsPIP_{\mu}PSPSPs$   
 $PIIPsPrC\grave{I}C, CH PSPsC\grave{H}P^{\circ}PrC\grave{H}P_{\mu}PSP^{\circ}P \gg C - PS P^{\circ}P \pm Ps PrPsP\acute{I}P^{\circ}PjC - PS. PhC\acute{I}P\acute{e}C - P \gg CHPeP\ddot{e}$   
 $C\acute{I}P\acute{I}P_{\mu}C\ddot{I}P\ddot{e}C,, C - C\ddot{I}PSP\ddot{e}PN_{\acute{e}} P^{\circ}PSC, P\ddot{e}PrPsC, PSP_{\mu}PIC - PrPsPjP\ddot{e}PN_{\acute{e}}, P\acute{I}C\grave{H}P\ddot{e} P \gg C - PeC\acute{r}PIP^{\circ}PSPSC -$   
 $C - PSC\acute{E}P\ddot{e}C \dots PiPsP \pm C - C\ddot{I}PSP\ddot{e}C \dots C\grave{H}P_{\mu}P^{\circ}PeC\ddot{I}C - PN_{\acute{e}} C\acute{I}P \gg C - Pr PeP_{\mu}C\grave{H}C\acute{r}PIP^{\circ}C, P\ddot{e}C\acute{I}C\grave{I}$   
 $PSP^{\circ}PN_{\acute{e}}P \pm C - P \gg CHC\acute{E} PIP\ddot{e}C\grave{H}P^{\circ}P\grave{I}P_{\mu}PSP\ddot{e}PjP\ddot{e} C\acute{I}P\ddot{e}PjP\acute{I}C, PsPjP^{\circ}PjP\ddot{e}.$

### **$P_{\mu}PsP \pm C - C\ddot{I}PSC - C\grave{H}P_{\mu}P^{\circ}PeC\ddot{I}C - C -$ .**

$P\acute{K}P\ddot{e}P\grave{I}C\ddot{I}P_{\mu} PSP^{\circ}PIP_{\mu}PrP_{\mu}PSPs PiP_{\mu}C\grave{H}P_{\mu}P \gg C - Pe PiPsP \pm C - C\ddot{I}PSP\ddot{e}C \dots C\grave{H}P_{\mu}P^{\circ}PeC\ddot{I}C - PN_{\acute{e}},$   
 $PIP\ddot{e}P \cdot PSP^{\circ}C\ddot{I}P_{\mu}PSP\ddot{e}C \dots C\acute{r} P\acute{I}C\grave{H}PsC\ddot{I}P_{\mu}C\acute{I}C - PeP \gg C - PSC - C\ddot{I}PSP\ddot{e}C \dots PrPsC\acute{I}P \gg C - PrP\grave{I}P_{\mu}PSC\ddot{H}$   
 $P\acute{I}C\grave{H}P\ddot{e} P \cdot P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC - PSC - PjPsPrP\ddot{e}PiC - PSC\acute{r} P \cdot P^{\circ} PiPsPeP^{\circ}P \cdot P^{\circ}PSPSC\grave{I}Pj$   
 $B \ll C\acute{I}C\acute{r}P \pm P^{\circ}C\grave{H}P^{\circ}C \dots PSPsC - PrP^{\circ}P \gg CH\ddot{H}PSP\ddot{e}PN_{\acute{e}} PeC\grave{H}PsPIPsPIP\ddot{e}P \gg P\ddot{e}PI PIPSP^{\circ}C\acute{I}P \gg C - PrPsPe$   
 $C\grave{H}PsP \cdot C\grave{H}P\ddot{e}PIC\acute{r} P^{\circ}PSP_{\mu}PIC\grave{H}P\ddot{e}P \cdot PjP\ddot{e}B \gg, C\grave{I}PeC - P \cdot P^{\circ} C\ddot{I}P^{\circ}C\acute{I}C, PsC, PsC\grave{H}$   
 $C\grave{H}PsP \cdot PiPsPrC - P \gg P_{\mu}PSPs P \cdot P^{\circ} PSP^{\circ}C\acute{I}C, C\acute{r}PiPSP\ddot{e}PjP\ddot{e} PeP^{\circ}C, P_{\mu}PiPsC\grave{H}C - C\grave{I}PjP\ddot{e}: PrC\acute{r}P\grave{I}P_{\mu}$   
 $C\ddot{I}P^{\circ}C\acute{I}C, Ps (\geq 1/10), C\ddot{I}P^{\circ}C\acute{I}C, Ps (\geq 1/100, < 1/10), PSP_{\mu}C\ddot{I}P^{\circ}C\acute{I}C, Ps (\geq 1/1000, \leq 1/100),$   
 $C\grave{H}C - PrPePs (\geq 1/10000, \leq 1/10000), PrC\acute{r}P\grave{I}P_{\mu} C\grave{H}C - PrPePs (< 1/10000), C\ddot{I}P^{\circ}C\acute{I}C, PsC, P^{\circ}$   
 $PSP_{\mu}PIC - PrPsPjP^{\circ} (PSP_{\mu}PjPsP\grave{I}P \gg P\ddot{e}IPs PIP\ddot{e}P \cdot PSP^{\circ}C\ddot{I}P\ddot{e}C, P\ddot{e} PSP^{\circ} PsC\acute{I}PSPsPIC -$   
 $PSP^{\circ}C\grave{I}PIPSP\ddot{e}C \dots PrP^{\circ}PSP\ddot{e}C \dots).$

$Pj PePsP\grave{I}PSC - PN_{\acute{e}} PiC\grave{H}C\acute{r}PiC - P \cdot P^{\circ} C\ddot{I}P^{\circ}C\acute{I}C, PsC, PsC\grave{H} PiPsP \pm C - C\ddot{I}PSC - C\grave{H}P_{\mu}P^{\circ}PeC\ddot{I}C - C -$   
 $P\acute{I}C\grave{H}P_{\mu}PrC\acute{I}C, P^{\circ}PIP \gg P_{\mu}PSPs C\acute{r} PiPsC\grave{H}C\grave{I}P\ddot{e}PrPeC\acute{r} P \cdot PjP_{\mu}PSC\acute{E}P_{\mu}PSPSC\grave{I}$   
 $C\acute{I}P_{\mu}C\grave{H}PN_{\acute{e}}PsP \cdot PSPsC\acute{I}C, C -.$

$P - P \pm PsPeC\acute{z} PeC\grave{H}PsPIC - C, P^{\circ} P \gg C - PjC,, P^{\circ}C, P\ddot{e}C\ddot{I}PSPsC - C\acute{I}P\ddot{e}C\acute{I}C, P_{\mu}PjP\ddot{e}: PSP_{\mu}C\ddot{I}P^{\circ}C\acute{I}C, Ps B\grave{H}''$   
 $C, C\grave{H}PsPjP \pm PsC\ddot{I}P\ddot{e}C, PsPiP_{\mu}PSC - C\grave{I}.$

$P - P \pm PsPeC\acute{z} C - PjC\acute{z}PSPSPsC - C\acute{I}P\ddot{e}C\acute{I}C, P_{\mu}PjP\ddot{e}: PSP_{\mu}C\ddot{I}P^{\circ}C\acute{I}C, Ps B\grave{H}'' P^{\circ}P \gg P_{\mu}C\grave{H}PiC - C\ddot{I}PSP^{\circ}$   
 $C\grave{H}P_{\mu}P^{\circ}PeC\ddot{I}C - C\grave{I}, PIP\ddot{e}C\acute{I}P\ddot{e}PiP^{\circ}PSPSC\grave{I}.$

$P - P \pm PsPeC\acute{z} PSP_{\mu}C\grave{H}PIPsPIPsC - C\acute{I}P\ddot{e}C\acute{I}C, P_{\mu}PjP\ddot{e}: PSP_{\mu}C\ddot{I}P^{\circ}C\acute{I}C, Ps B\grave{H}'' PiPsP \gg PsPIPSP\ddot{e}PN_{\acute{e}}$   
 $P \pm C - P \gg CH.$

$P - P \pm PsPeC\acute{z} C\acute{I}P_{\mu}C\grave{H}C\ddot{I}C\grave{I}: PSP_{\mu}C\ddot{I}P^{\circ}C\acute{I}C, Ps B\grave{H}'' C, P^{\circ}C \dots C - PeP^{\circ}C\grave{H}PrC - C\grave{I}; C\grave{H}C - PrPePs B\grave{H}''$   
 $P \pm C\grave{H}P^{\circ}PrP\ddot{e}PeP^{\circ}C\grave{H}PrC - C\grave{I}.$

$P - P \pm PsPeC\acute{z} C\acute{I}C\acute{z}PrP\ddot{e}PSPSPsC - C\acute{I}P\ddot{e}C\acute{I}C, P_{\mu}PjP\ddot{e}: PSP_{\mu}C\ddot{I}P^{\circ}C\acute{I}C, Ps B\grave{H}''$   
 $P^{\circ}C\grave{H}C, P_{\mu}C\grave{H}C - P^{\circ}P \gg CH\ddot{H}PSP^{\circ} PiC - PiPsC, P_{\mu}PSP \cdot C - C\grave{I}, PIP^{\circ}P \cdot PsPrP\ddot{e}P \gg P^{\circ}C, P^{\circ}C\ddot{I}C - C\grave{I}.$

$P - P \pm PsPeC\acute{z} C, C\grave{H}P^{\circ}PIPSPsC - C\acute{I}P\ddot{e}C\acute{I}C, P_{\mu}PjP\ddot{e}: PSP_{\mu}C\ddot{I}P^{\circ}C\acute{I}C, Ps B\grave{H}'' PSC\acute{r}PrPsC, P^{\circ};$   
 $C\grave{H}C - PrPePs B\grave{H}'' PeP\ddot{e}C\acute{E}PePsPIP^{\circ} PSP_{\mu}PiC\grave{H}PsC \dots C - PrPSC - C\acute{I}C, CH.$

$P - P \pm PsPeC\acute{z} PiP_{\mu}PiP^{\circ}C, PsP \pm C - P \gg C - P^{\circ}C\grave{H}PSPsC - C\acute{I}P\ddot{e}C\acute{I}C, P_{\mu}PjP\ddot{e}: C\grave{H}C - PrPePs B\grave{H}''$   
 $C, C\grave{H}P^{\circ}PSP \cdot P\ddot{e}C, PsC\grave{H}PSP_{\mu} PiC - PrPIP\ddot{e}C\% P_{\mu}PSPSC\grave{I} P^{\circ}PeC, P\ddot{e}IPSPsC\acute{I}C, C -$   
 $C,, P_{\mu}C\grave{H}PjP_{\mu}PSC, C - PI PiP_{\mu}C\ddot{I}C - PSPeP\ddot{e}.$

$P - P \pm PsPeC\acute{z} PsC\grave{H}PiP^{\circ}PSC - PI PrP\ddot{e}C \dots P^{\circ}PSPSC\grave{I}, PiC\grave{H}C\acute{z}PrPSPsC - PeP \gg C - C, PeP\ddot{e} C, P^{\circ}$   
 $C\acute{I}P_{\mu}C\grave{H}P_{\mu}PrPsC\acute{I}C, C - PSPSC\grave{I}: PSP_{\mu}PIC - PrPsPjPs B\grave{H}'' PiC - PiPsPeC\acute{I}C - C\grave{I}.$

***PŷPµCḡPjC-PS PİCḡPëPrP°C,PSPsCÍC,C-.*** 3 CḡPsPePë.

**PJPjPsPIPë P•P±PµCḡC-PiP°PSPSCİ.**

P—P±PµCḡC-PiP°C,Pë Pİ PsCḡPëPiC-PSP°P»CHḡPSC-PNë CÍPİP°PePsPIC†C- PİCḡPë  
C,PµPjPİPµCḡP°C,CÍCḡC- PSPµ PIPëC‰Pµ 25 B°Pŷ, CÍ P•P°C...PëC‰PµPSPsPjCÍ PIC-Pr  
CÍPIC-C,P»P° PjC-CÍC†C-.

P—P±PµCḡC-PiP°C,Pë CÍ PSPµPrPsCÍC,CÍPİPSPsPjCÍ PrP»Cİ PrC-C,PµPNë PjC-CÍC†C-.

**PJPİP°PePsPIPëP°.**

PµPs 10 C,P°P±P»PµC,PsPe, PIPëCḡPëC,PëC... PİP»C-PIPePsPIPsCḡ PsP±PsP»PsPSPëPsCḡ, CÍ  
P±P»C-CÍC,PµCḡC-; PİPs 3 P±P»C-CÍC,PµCḡPë CÍ PeP°CḡC,PsPSPSC-PNë PİP°C†C†C-.

**PŷP°C,PµPiPsCḡC-Cİ PIC-PrPİCÍCÍPeCÍ.** P—P° CḡPµC†PµPİC,PsPj.

**P’PëCḡPsP±PSPëPe.**

PḡPSC,,P°CḡPj P•P»P»P°CÍ Pŷ.Pḡ.

**PḡC-CÍC†PµP•PSP°C...PsPrP¶PµPSPSCİ PIPëCḡPsP±PSPëPeP° C,P° P°PrCḡPµCÍP°  
PjC-CÍC†Cİ PİCḡPsPIP°PrP¶PµPSPSCİ PNëPsPiPs PrC-CİP»CHḡPSPsCÍC,C-.**

61-PNë PePj PķP°C†C-PsPSP°P»CHḡPSPsC— PrPsCḡPsPiPë PḡC,,C-PSPë-P»PjC-Cİ,  
PŷC...C-PjP°C,P°CḡC- P’C-PsC,C-P°CÍ, 32009, P’CḡPµC†C-Cİ.