

IPKPYPP PJPbP|P+PI

P+P»C PjPµP+PëC+PSPsPiPs P·P°CÍC,PsCÍC+PIP°PSPSC P»C-PeP°CÍCHPePsPiPs P·P°CÍPsP±Cí

PkP+PyPhPµP+Pk

(NITOPIN^{B®})

PyPeP»P°Pr:

PrC-CHC+P° CHPµC+PsPIPëPSP°: nimodipine;

1 C,P°P±P»PµC,PeP°, PIPeCHPeC,P° PíP»C-PIPePsPIPsCH PsP±PsP»PsPSPePsCH,
PjC-CÍC,PëC,CH PSC-PjPsPrPëPiC-PSCr 30 PjPi;

*PrPsPiPsPjC-P PSC- CHPµC+PsPIPëPSPë: C+PµP»CHP»PsP·P°
PjC-PeCHPsPeCHPëCÍC,P°P»C-C+PSP°, PeCHPsC...PjP°P»CH PeCíPeCíCHCíPrP·C PSPëPN,
PíPsP»C-PIC-PrPsPS, PeCHPsCÍPíPsPIC-PrPsPS, PjP°PiPSC-CH CÍC,PµP°CÍP°C,;*

*PsP±PsP»PsPSPeP°: PiC-PíCHPsPjPµP»PsP·P°, PjP°PeCHPsPiPsP» 4000, C,PëC,P°PSCr
PrC-PsPeCÍPëPr (E 171).*

**P»C-PeP°CÍCHPeP° C,,PsCHPjP°. PyP°P±P»PµC,PePë, PIPeCHPeC,C- PíP»C-PIPePsPIPsCH
PsP±PsP»PsPSPePsCH.**

*PhCÍPSPsPIPS- C,,C-P·PëPePs-C...C-PjC-C+PSC- PIP»P°CÍC,PëPIPsCÍC,C-: P±C-P»C- P°P±Ps
P PPsPIC,CíPIP°C,C- PrPIPsPsPíCíPeP»C- C,P°P±P»PµC,PePë.*

P»P°CÍPjP°PePsC,PµCHP°PíPµPIC,PëC+PSP° PiCHCíPíP°.

*PYpµP»PµPeC,PëPIPS- P±P»PsPeP°C,PsCHPë PeP°P»CHC+C-C"PIPëC... PeP°PSP°P»C-PI P·
PíPµCHPµPIP°P PSPëPj PíPíP»PëPIPsPj PSP° CÍCíPrPëPSPë. PµPsC...C-PrPSC-
PrPëPiC-PrCHPsPiC-CHPëPrPëPSCr. PkC-PjPsPrPëPiC-PS.*

PµPsPr PhPyPI C08C A06.

P»P°CÍPjP°PePsP»PsPiC-C+PSC- PIP»P°CÍC,PëPIPsCÍC,C-.

P»P°CÍPjP°PePsPrPëPSP°PjC-PeP°.

*PkC-PjPsPrPëPiC-PS C" P±P»PsPeP°C,PsCHPsPj PeP°P»CHC+C-C"PIPëC... PeP°PSP°P»C-PI
PrPëPiC-PrCHPsPiC-CHPëPrPëPSPsPIPsC— PiCHCíPíPë P· PíPµCHPµPIP°P PSPëPj PíPíP»PëPIPsPj
PSP° CÍCíPrPëPSPë PiPsP»PsPIPSsPiPs PjPsP·PeCí. PkC-PjPsPrPëPiC-PS P·P±C-P»CHC€CíC"*

C†PμCḡPμP±CḡP°P»CHBPSCř 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»CHBPSPsPiPs P·P°CłC,PsCłCřPIP°PSPSCł
P»C-PeP°CḡCłCHPePēPNē P·P°CłC-P± C€PIPēPrPePs PICłPjPsPeC,CřCḡC,CHCłCł.
PḡP°PeCłPēPjP°P»CHBPSP° 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»CHBPSPsPiPs 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, PrPIPsPeP°PjPμCḡPSP°
PjPsPrPμP»CH) PīCḡPē PIPSCřC,CḡC-C€PSCḡPsPIPμPSPSPsPjCř PIPμPrPμPSPSC-
PrPsCḡC-PIPSḡCḡ 0,9Bḡ“2,3 P»/PePi PjP°CłPē C,C-P»P°. P—P°PiP°P»CHBPSPēPNē
(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 PIPēPIPsPrPēC,CHCłCł Cř
PIPēPiP»CłPrC- PjPμC,P°P±PsP»C-C,PI, C%Ps CřC,PIPsCḡCḡCḡC,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»CḡPIP°PSPSCł. PhPePēCłPSPμ CḡPsP·C%PμPīP»PμPSPSCł PμC,,C-CḡCř,
PiC-PrCḡPsPeCłPēP»CḡPIP°PSPSCł 2- C,P° 6-PjPμC,PēP»-PiCḡCřPī C,P°
PīP»CḡPeCřCḡPsPSC-P·P°C†C-Cł CłPe CḡPμP°PeC†C-Cł PePsPSBḡ™CḡPiP°C†C-C— Cḡ
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»CḡPrPēPSPē P·PrC-PNēCłPSCḡCḡC,CHCłCł PSP° 50 %
PSPēCḡPeP°PjPē C,P° PSP° 30 % C-P· P¶PsPIC†Cḡ.

PμCḡPē PīPμCḡPsCḡP°P»CHBPSPsPjCř P·P°CłC,PsCłCřPIP°PSPSC- PjP°PeCłPēPjP°P»CHBPSP°

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 PīPsPrPēPSPē. PḡPμCḡPjC-PSP°P»CHPSPēPN°
PīPμCḡC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCḡ 5Bḡ“10 PīPsPrPēPS PSPμ C”
CḡPμP»PμPIP°PSC,PSPēPj PrP»Cḡ PICḡC,P°PSPsPIP»PμPSPSCḡ
CḡPμPePsPjPμPSPPrPsPIP°PSPsPīPs C-PSC,PμCḡPIP°P»Cḡ PjC-Pḡ PīCḡPēPN°PsPjPsPj PrPsP·
P»C-PeP°CḡCḡCHPePsPīPs 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»PsPīC-C‡PSPēC... CḡPsP·P»P°PrC-PI PīC-CḡP»Cḡ
CḡCḡP±P°CḡP°C...PSPsC—PrP°P»CHPSPsPīPs 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°CḡCḡCHPePsPīPs P·P°CḡPsP±Cḡ.

PμC-Pr C‡P°Cḡ C,P° PIPīCḡPsPrPsPIPḡ PsPrPSPsPīPs 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°CḡCḡCHPePsPīPs 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°CḡCfCḡCHPeC- 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°CḡCfCḡCHPePëPjPë 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»CHPSPs 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°CḡCfCḡCHPePsPiPs 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°CḡCfCḡCHPeC- P·P°CfPsP±Pë.

PḡPrPSPsC†P°CfPSPμ P·P°CfC,PsCfCfPIP°PSPSCḡ PiP°C†C-C”PSC,P°Pj P»C-C,PSCHPsPiPs 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-PSCHPIP°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»CHPSPëPj PeCḡPsPIPsPiPëP»PëPiPsPj, Cḡ 4 CḡP°P·Pë PiPμCḡPμPiPëC%CḡC” PrPsP·Cḡ, C%Ps P·P°CfC,PsCfPsPICḡPIP°P»P°CḡCḡ Cḡ C†CHPsPjCḡ 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»CHPSPsPiPs 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°CḡCfCḡCHPePëPjPë 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»CHPSPëPḡ 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⁺PsC⁺P° C,,PsC⁺PjP°P»CH⁺PsC- PrPsC⁺P»C-PrP⁺PI⁺PμPSPSC⁺ PrP»C⁺ PIP⁺PI⁺C⁺PI⁺PμPSPSC⁺ P⁺PsC,PμPSC⁺C-PN⁺PSPsC— PIP·P°C”PjPsPrC-C— PjC-P⁺ PSC-PjPsPrP⁺PiC-PSPsPj C,P° C⁺P⁺PjP⁺ P»C-PeP°C⁺CH⁺PeP⁺PjP⁺ P·P°C⁺PsP±P°PjP⁺ PSPμ P⁺C⁺PsPIPsPrP⁺P⁺»P⁺C⁺CI, PSPμ PjPsP⁺PI⁺P° PIP⁺PeP»C⁺CH⁺CH⁺PeC,P⁺ PN⁺PjPsPIC-C⁺PsC-C⁺CH⁺ P·P±C-P»CH⁺CH⁺PePμPSPSC⁺ P⁺P»P°P·PjPsPI⁺PeC... PePsPSC⁺PμPSC,C⁺PsP°C⁺C-PN⁺ PSC-PjPsPrP⁺PiC-PSC⁺ (PrP⁺PI. C⁺PsP·PrC-P» B«PhC⁺PsP±P»P⁺PIPsC⁺C, C- P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺IB»).

P⁺hP·P⁺CH⁺PsPjC-C⁺P⁺PS C...PsC⁺P° C- PSP°P»PμP⁺PI⁺PeC,CH⁺ P·P° C⁺C,C⁺CH⁺CH⁺PeC,C⁺CH⁺PsC⁺ PrPs PeP»P°C⁺C⁺ PjP°PeC⁺PsP»C-PrPSP⁺PeC... P°PSC,P⁺PeP±C-PsC,P⁺PeC-PI, PSPμ C” C-PSPI⁺C-P±C-C,PsC⁺PsPj CYP3A4.

PhPrPSPsC⁺P°C⁺PI⁺PSPμ P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺ P⁺P°C⁺C-C”PSC,P°Pj P»C-C,PSCH⁺PsPiPs PIC-PeC⁺ PSC-PjPsPrP⁺PiC-PSC⁺ C⁺ PrPsP·C- 30 PjPi 2 C⁺PsP°P·P⁺ PSP° PrPsP±C⁺ C,P° P°PSC,P⁺PrPμP⁺PI⁺C⁺PI⁺P°PSC,C⁺ C,,P»C⁺PsPeC⁺PI⁺C,P⁺PePSC⁺ 20 PjPi PSP° PrPsP±C⁺ P⁺PI⁺CH⁺PeP·PIPsPrP⁺P⁺Ps PrPs P⁺PI⁺PeC%PμPSPSC⁺ C⁺CH⁺-PI⁺PS⁺ PSC-PjPsPrP⁺PiC-PSC⁺ C⁺ P⁺P»P°P·PjC- PeC⁺PsPIC- PjP°PN⁺P⁺PI⁺Pμ PSP° 50 % C,P° P·PSP°C⁺PS⁺SiPs P·PSP⁺PI⁺PμPSPSC⁺ C⁺CH⁺-PI⁺PS⁺ C,,P»C⁺PsPeC⁺PI⁺C,P⁺PePSC⁺ P±PμP· PIP⁺P»P⁺PI⁺C⁺ PSP° PN⁺PsPiPs P°PeC,P⁺PI⁺PS⁺PePN⁺ PjPμC,P°P±PsP»C-C, PSPsC⁺CH⁺,P»C⁺PsPeC⁺PI⁺C,P⁺PS (PrP⁺PI. C⁺PsP·PrC-P» B«PhC⁺PsP±P»P⁺PIPsC⁺C, C- P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺IB»).

PhPrPSPsC⁺P°C⁺PI⁺PSPμ P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺ PSC-PjPsPrP⁺PiC-PSC⁺ P· P⁺CH⁺PsC,P⁺CH⁺C⁺PrPsPjPSP⁺PePj P»C-PeP°C⁺CH⁺CH⁺PeP⁺Pj P·P°C⁺PsP±PsPj (PIP°P»CH⁺PI⁺CH⁺PsC”PI⁺ PeP⁺CH⁺P»PsC,P°) P°P±Ps P°PSC,P°PiPsPSC-C⁺C,PsPj H₂-C⁺PI⁺C⁺PI⁺C,PsC⁺CH⁺-PI (C⁺P⁺PePjPμC,P⁺PrP⁺PS) PjPsP⁺PI⁺Pμ P⁺CH⁺PeP·PI⁺PI⁺C⁺C,P⁺ PrPs P·P±C-P»CH⁺CH⁺PePμPSPSC⁺ P⁺P»P°P·PjPsPI⁺PsC— PePsPSC⁺PμPSC,C⁺PsP°C⁺C-C— PSC-PjPsPrP⁺PiC-PSC⁺ (PrP⁺PI. C⁺PsP·PrC-P» B«PhC⁺PsP±P»P⁺PIPsC⁺C, C- P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺IB»).

P—PI⁺P°P⁺PI⁺C⁺PeP PSP° PrPsC⁺PI⁺C-Pr P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺ P°PSC,P°PiPsPSC-C⁺C,P° PeP°P»CH⁺C⁺C-CH⁺ PSC-C,,PμPrP⁺PiC-PSC⁺, PsPrPSPsC⁺P°C⁺PI⁺PSPμ P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺ P· C...C-PSC⁺PI⁺CH⁺PeC⁺C,P⁺PePSPsPj/PrP°P»CH⁺C,,PsP⁺CH⁺PeC⁺C,P⁺PePSPsPj PjPsP⁺PI⁺Pμ P⁺CH⁺PeP·PI⁺PI⁺C⁺C,P⁺ PrPs P·P±C-P»CH⁺CH⁺PePμPSPSC⁺ P⁺P»P°P·PjPsPI⁺PeC... PePsPSC⁺PμPSC,C⁺PsP°C⁺C-PN⁺ PSC-PjPsPrP⁺PiC-PSC⁺ (PrP⁺PI. C⁺PsP·PrC-P» B«PhC⁺PsP±P»P⁺PIPsC⁺C, C- P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺IB»).

P⁺PI⁺P»P⁺PI PSC-PjPsPrP⁺PiC-PSC⁺ PSP° C-PSC⁺CH⁺- P»C-PeP°C⁺CH⁺CH⁺PeC- P·P°C⁺PsP±P⁺Pe

Pj PrPsC⁺P»C-PrP⁺PI⁺PμPSPSC⁺IC... PSP° C,PI⁺P°C⁺PePSP°C... PIC⁺C,P°PSPsPI⁺PμPSPs, C%Ps PsPrPSPsC⁺P°C⁺PI⁺PSPμ P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC⁺ PSC-PjPsPrP⁺PiC-PSC⁺ C,P° P·P⁺PrPsPIC⁺PrP⁺PePSC⁺ P⁺CH⁺PeP·PIPsPrP⁺PeC,CH⁺ PrPs P·P±C-P»CH⁺CH⁺PePμPSPSC⁺ AUC P·P⁺PrPsPIC⁺PrP⁺PePSC⁺ C,P° P·PjPμPSC⁺PePμPSPSC⁺ PN⁺PsPiPs PsP±P⁺PI⁺ C”PjC⁺ C⁺PsP·P⁺PsPrC-P»C⁺ PN⁺ PeP»C-C⁺PI⁺PS⁺C⁺C⁺. P⁺hP»C-PSC-C⁺PS⁺P° P·PSP°C⁺C⁺C%C-C⁺C,CH⁺ C⁺C-C”C— PIP·P°C”PjPsPrC-C— PSPμPIC-PrPsPjP°, P°P»Pμ, P·PI⁺P°P⁺PI⁺C⁺PeP PSP° PrPsP·PsP·P°P»PμP⁺PI⁺PS⁺PePN⁺ C...P°C⁺PsP°PeC,PμC⁺ P⁺CH⁺PsC,,C-P»CH⁺ P⁺PsP±C-C⁺PS⁺PeC... PμC,,PμPeC,C-PI P·P⁺PrPsPIC⁺PrP⁺PePSC⁺, C⁺CH⁺ PIP·P°C”PjPsPrC-CH⁺ C⁺P»C-Pr PIC⁺CH⁺P°C...PsPIC⁺PI⁺P°C,P⁺ C⁺ P⁺P°C⁺C-C”PSC,C-PI, C⁺PeC- PsPrPSPsC⁺P°C⁺PI⁺PSPs PsC,C⁺PePjC⁺CH⁺C,CH⁺ PSC-PjPsPrP⁺PiC-PS C,P° P·P⁺PrPsPIC⁺PrP⁺PS.

P⁺PS⁺CH⁺- C,P⁺PeP⁺ PIP·P°C”PjPsPrC-PN⁺

P”C-P⁺PsC,PμPSP·P⁺PI⁺PS- P»C-PeP°C⁺CH⁺CH⁺PeC- P·P°C⁺PsP±P⁺Pe.

PμC⁺Pe P⁺PrPSPsC⁺P°C⁺PI⁺PSPsPjC⁺ P·P°C⁺C,PsC⁺C⁺PI⁺P°PSPSC- PSC-PjPsPrP⁺PiC-PS PjPsP⁺PI⁺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,);
- A₁-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%oPs 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. PĤPe
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,PsPIPsiPs
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%oC-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,,PsChPjC- C,P°P±P»PµC,PsPe PSPµ CfP»C-Pr PsPrPSPsC±P°CfPSPs
P·P°CfC,PsCfPSPICrPIP°C,Pë P· ChPSP·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°ChP°C...PSPsC—PrP°P»CHPSPëPj PeChPSPsPIPsPIPëP»PëPIPsPj PIPSP°CfP»C-PrPsPe
C,ChP°PIPjPë, PsCfPeC-P»CHPePë PSPµ PICfC,P°PSPsPIP»PµPSPëPN
CfPiChPëCII,C,P»PëPIPëPN PiChPSC,,C-P»CH CfPiC-PIPIC-PrPSPsCëPµPSPSCII
PePsChPëCfC,CH/ChPëP·PëPe C,P° PrP»CII C†CHPsPiPs PiPsPeP°P·P°PSPSCII PSPµ
PjPsP¶CfC,CH P±CfC,Pë PIPëP·PSP°C±PµPSC- CfPiPµC†PëC,,C-C±PSC- PiChCfPiPë
PiP°C†C-C"PSC,C-PI, CIIPeC- P± PsC,ChPëPjCfPIP°P»Pë PePsChPëCfC,CH.

PkC-C,PsPiC-PS CfP»C-Pr P· PsP±PµChPµP¶PSC-CfC,Ch P·P°CfC,PsCfPSPICrPIP°C,Pë
PiP°C†C-C"PSC,P°Pj C-P· PSP°P±ChCIIPePsPj PjPsP·PeCf P°P±Ps PiC-PrPIPëC%PµPSPSCII
PIPSCfC,ChC-CëPSCHPsC±PµChPµPiPSPsPiPs C,PëCfPeCf C,CII¶PePsPiPs CfC,CfPiPµPSCII.
PIPsC±P° PSPµ P±CfP»Ps PiChPSPPrPµPjPsPSCfC,ChPSPIP°PSPs, C%Ps P»C-PeCfPIP°PSPSCII
P»C-PeP°ChCfCHPePëPj P·P°CfPSP±PsPj PkC-C,PsPiC-PS P°CfPSC†C-CHC"C,CHCfCII P·
PiC-PrPIPëC%PµPSPSCII Pj PIPSCfC,ChC-CëPSCHPsC±PµChPµPiPSPsPiPs C,PëCfPeCf, Cr
C,P°PePëC... PIPëPiP°PrPeP°C... P°P±Ps PiChPë PiC-PrPIPëC%PµPSPSC- PIPjC-CfC,Cf PIPsPrPë
Cf C,PeP°PSPëPSP°C... PjPsP·PeCf (PiPµPSPµChP°P»C-P·PsPIP°PSPëPN PSP°P±ChCIIPe
PiPsP»PsPIPSPsPiPs PjPsP·PeCf) ChPµPePsPjPµPSPPrCfC"C,CHCfCII ChPµC,PµP»CHPSPëPN
PePsPSC,ChPSP»CH CfC,P°PSCr PiP°C†C-C"PSC,P°.

PŸP»C-Pr PrPsC,ChPëPjCfPIP°C,PëCfCII PsP±PµChPµP¶PSPsCfC,C- PiChPë
P»C-PeCfPIP°PSPSC- PiP°C†C-C"PSC,C-PI P· P°ChC,PµChC-P°P»CHPSPsCh
PiC-PiPsC,PµPSP·C-C"Ch (CfPëCfC,PsP»C-C±PSPëPN C,PëCfPe PjPµPSCëPµ 100 PjPj ChC,,
CfC,,).

Pj PiP°C†C-C"PSC,C-PI C-P· C†PëChPSP·PsPj PiPµC±C-PSPePë, CIIPeC- PsC,ChPëPjCfChC,CH
PkC-C,PsPiC-PS, PjPsP¶Pµ P·PSPëP¶CfPIP°C,PëCfCII PeP»C-ChPµPSCf
P»C-PeP°ChCfCHPePsPiPs P·P°CfPSP±Cf, C,PsPjCf Cr C,P°PePëC... PiP°C†C-C"PSC,C-PI
ChPµPePsPjPµPSPPrCfC"C,CHCfCII ChPµC,PµP»CHPSPëPN PePsPSC,ChPSP»CH
P°ChC,PµChC-P°P»CHPSPsPiPs C,PëCfPeCf.

PkC-PjPsPrPëPiC-PS PjPµC,P°P±PsP»C-P·CfC"C,CHCfCII PµPSP·PëPjPSPsCh
CfPëCfC,PµPjPsCh C†PëC,PsC...ChPSPjCf P450 3A4. P»C-PeP°ChCfCHPeC- P·P°CfPSP±Pë,
PIC-PrPsPjC- CIIPe C-PSPiC-P±C-C,PsChPë P°P±Ps C-PSPrCfPeC,PsChPë C†C-C"C—
PµPSP·PëPjPSPsC— CfPëCfC,PµPjPë, PjPsP¶CfC,CH PIPiP»PëPIP°C,Pë PSP°
PiChPµCfPëCfC,PµPjPSPëPN PjPµC,P°P±PsP»C-P·Pj P°P±Ps P·PjC-PSCHPIP°C,Pë
PeP»C-ChPµPSCf PSC-PjPsPrPëPiC-PSCr (PrPëPI. ChPSP·PrC-P»Pë B«P·P·P°C"PjPsPrC-CII P·
C-PSCëPëPjPë P»C-PeP°ChCfCHPePëPjPë 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· PiPsChCfCëPµPSPSCII PjPë C,,CfPSPeC†C-C— PiPµC±C-PSPePëB»).

P"Ps P»C-PeP°ChCfCHPePëC... P·P°CfPSP±C-PI, PIC-PrPsPjPëC... CIIPe C-PSPiC-P±C-C,PsChPë
PµPSP·PëPjCf C†PëC,PsC...ChPSPjCf P450 3A4 C- C%Ps PjPsP¶CfC,CH CfPiChPëC±PëPSCII,C,Pë
P·P±C-P»CHCëPµPSPSCII PiP»P°P·PjPsPIPëC... PePsPSC†PµPSC,ChP°C†C-PN
PSC-PjPsPrPëPiC-PSCr, PSP°P»PµP¶P°C,CH:

- PjP°PeChPSP»C-PrPSC- P°PSC,PëP±C-PsC,PëPePë (PSP°PiChPëPeP»P°Pr
PµChPëC,ChPSPjC-C†PëPS);

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

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

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

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

$\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 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 P}\eta\text{C}-\text{PSPeP}^{\circ}\text{Pj PSP}\mu\text{PiC}\eta\text{PsPiPsPrP}\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 PIPiP}\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 PIPiP}\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{r}}\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 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 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}}.$

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

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

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

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

PiPsC7CfC€PµPSPSC¶ C,,CfPSPeC†C-C— CfPiPµC7PjPë. PkPµPIC-PrPsPjPs,
PSP°CfPeC-P»CHPePë P·PSP°C†CfC%PëPjPë C” C†C- P·PjC-PSPë PiC7Pë
PePsC7PsC,PePsC,C7PëPIP°P»PsPjCf P»C-PeCfPIP°PSPSC-.

P—PrP°C,PSC-CfC,CH PIPiP»PëPIP°C,Pë PSP° C€PIPëPrPeC-CfC,CH C7PµP°PeC†C-C— PiC7Pë
PePµC7C¿PIP°PSPSC- P°PIC,PsC,C7P°PSCfPiPsC7C,PsPj P°P±Ps C-PSC€PëPjPë
PjPµC...P°PSC-P·PjP°PjPë.

P—PrP°C,PSC-CfC,CH PiP°C†C-C”PSC,P° PePµC7CfPIP°C,Pë P°PIC,PsC,C7P°PSCfPiPsC7C,PsPj
P°P±Ps PiC7P°C†CHPIP°C,Pë P· C-PSC€PëPjPë PjPµC...P°PSC-P·PjP°PjPë PjPsP¶Pµ P±CfC,Pë
PiPsC7CfC€PµPSP° Cf P·PiB7™ C¶P·PeCf P· PjPsP¶P»PëPIPëPj PIPëPSPëPePSPµPSPSC¶Pj
P·P°PiP°PjPsC7PsC±PµPSPSC¶.

PŸPiPsCfC-P± P·P°CfC,PsCfC¿PIP°PSPSC¶ C,P° PrPsP·Pë.

PŸC¿P±P°C7P°C...PSPsC—PrP°P»CHPSPëPNë PeC7PsPIPsPIPëP»PëPI PIPSP°CfP»C-PrPsPe
C7PsP·C7PëPIC¿ P°PSPµPIC7PëP·PjPë

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° CfC,P°PSPsPIPëC,CH 2 C,P°P±P»PµC,PePë.
PµC7PëPNëPjP°C7C,CH P· C-PSC,PµC7PIP°P»P°PjPë 4 PiPsPrPëPSPë (P·P°PiP°P»CHPSP°
PrPsP±PsPIP° PrPsP·P° B7” 360 PjPi), P·P°PiPëPIP°C7C±Pë PIPsPrPsC7.
P—P°CfC,PsCfCfPIP°PSPSC¶ CfP»C-Pr C7PsP·PiPsC±P°C,Pë PIPiC7PsPrPsPIP¶ 4 PrPSC-PI
PiC-CfP»C¶ CfCfP±P°C7P°C...PSPsC—PrP°P»CHPSPsPiPs PeC7PsPIPsPIPëP»PëPICf,
C,C7PëPIP°P»C-CfC,CH PiC7PëPNëPsPjCf B7” 21 PrPµPSC7.

PJ C7P°P·C- PiC7PsPIPµPrPµPSPSC¶ PsPiPµC7P°C,PëPIPSPsPiPs PIC,C7CfC±P°PSPSC¶
P·P°CfC,PsCfCfPIP°PSPSC¶ P»C-PeP°C7CfCHPePsPiPs P·P°CfPsP±Cf PkC-C,PsPiC-PS
CfP»C-Pr PiC7PsPrPsPIP¶PëC,Pë (Cf P·P°P·PSP°C±PµPSPsPjCf PIPëC%Pµ PrPsP·CfPIP°PSPSC-)
PrPs P·P°PiPµC7C€PµPSPSC¶ 21-PrPµPSPSPsPiPs PiPµC7C-PsPrCf P»C-PeCfPIP°PSPSC¶.

PJ C7P°P·C- C7PsP·PIPëC,PeCf PiPsP±C-C±PSPëC... C7PµP°PeC†C-PNë P·P° PiPsC,C7PµP±Pë
CfP»C-Pr P·PjPµPSC€PëC,Pë PrPsP·Cf P°P±Ps PiC7PëPiPëPSPëC,Pë P»C-PeCfPIP°PSPSC¶.

PŸC¿P±P°C7P°C...PSPsC—PrP°P»CHPSPëPNë PeC7PsPIPsPIPëP»PëPI PIPSP°CfP»C-PrPsPe
C,C7P°PIPjPë

P—P°CfC,PsCfCfPIP°PSPSC¶ PSC-PjPsPrPëPiC-PSCf PSPµ C7PµPePsPjPµPSPPrCfC”C,CHCfC¶,
PsCfPeC-P»CHPePë PSPµ PICfC,P°PSPsPIP»PµPSPëPNë CfPiC7PëC¶C,P»PëPIPëPNë
PiC7PsC,,C-P»CH PePsC7PëCfC,CH/C7PëP·PëPe.

PµP°C†C-C”PSC,Pë P· PiPsC7C¿C€PµPSPSC¶PjPë C,,C¿PSPeC†C-C— PiPµC±C-PSPePë

PµC7Pë C,C¶P¶PePsPjCf PiPsC7CfC€PµPSPSC- C,,CfPSPeC†C-C— PiPµC±C-PSPePë,
P·PsPeC7PµPjP° PiC7Pë C†PëC7PsP·C- PiPµC±C-PSPePë, P±C-PsPrPsCfC,CfPiPSC-CfC,CH
PSC-PjPsPrPëPiC-PSCf PjPsP¶Pµ P·P±C-P»CHC€CfPIP°C,PëCfC¶ PIPSP°CfP»C-PrPsPe
P·PSPëP¶PµPSPSC¶ PiC7PµCfPëCfC,PµPjPSPsPiPs PjPµC,P°P±PsP»C-P·PjCf C,P°
PjPµC,P°P±PsP»C-C±PSPsPiPs PeP»C-C7PµPSCfCf. P”C-C¶ P»C-PeP°C7CfCHPePsPiPs
P·P°CfPsP±Cf C,P° PiPsP±C-C±PSC- C7PµP°PeC†C-C—, PSP°PiC7PëPeP»P°Pr
P·PSPëP¶PµPSPSC¶ P°C7C,PµC7C-P°P»CHPSPsPiPs C,PëCfPeCf, Cf C†PëC...

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

$P \cdot P^{\circ} C \dots C - Pr \ P_{\mu} PeCl^{\circ} C, C_{\eta} P_{\mu} P S P S C - C, P_{\mu} C_{\eta} P^{\circ} P i C - C - C_{\eta} P_{\mu} Pe P s P j P_{\mu} P S P r C r^{\circ} C, C_{\eta} C l^{\circ} C l$
 $P i C_{\eta} P s P j P e P i P^{\circ} P S P S C l C \epsilon P \gg C r^{\circ} P S P e P^{\circ} P \cdot P i P s P r P^{\circ} P \gg C_{\eta} C \epsilon P e P j \ P \cdot P^{\circ} C l^{\circ} C, P s C l^{\circ} C r^{\circ} P i P^{\circ} P S P S C l P j$
 $P^{\circ} P e C, P e P i P s P i P^{\circ} P S P s P i P s \ P i C r^{\circ} P i C - P \gg P \gg C l l. \ P_{\mu} C_{\eta} P e \ C l^{\circ} C r^{\circ} C, C, C^{\circ} P i P s P j C r^{\circ} P \cdot P S P e P \ P_{\mu} P S P S C -$
 $P^{\circ} C_{\eta} C, P_{\mu} C_{\eta} C - P^{\circ} P \gg C_{\eta} P S P s P i P s \ C, P e C l^{\circ} P e C r^{\circ} P i P S C r^{\circ} C, C_{\eta} C - C \epsilon P S C_{\eta} P s P i P_{\mu} P S P S P s$
 $P i P i P s P r C l l C, C_{\eta} P S P s C_{\eta} P^{\circ} P r C_{\eta} P_{\mu} P S P^{\circ} P \gg C - P S \ P^{\circ} P \pm P s \ P r P s P i P^{\circ} P j C - P S. \ P_{\eta} C l^{\circ} P e C - P \gg C_{\eta} P e P e$
 $C l^{\circ} P i P_{\mu} C \dagger P e C, C - C \dagger P S P e P N_{\epsilon} \ P^{\circ} P S C, P e P r P s C, \ P S P_{\mu} P i C - P r P s P j P e P N_{\epsilon}, \ P i C_{\eta} P e \ P \gg C - P e C r^{\circ} P i P^{\circ} P S P S C -$
 $C - P S C \epsilon P e C \dots \ P i P s P \pm C - C \dagger P S P e C \dots \ C_{\eta} P_{\mu} P^{\circ} P e C \dagger C - P N_{\epsilon} \ C l^{\circ} P \gg C - P r \ P e P_{\mu} C_{\eta} C r^{\circ} P i P^{\circ} C, P e C l^{\circ} C l$
 $P S P^{\circ} P N_{\epsilon} P \pm C - P \gg C_{\eta} C \epsilon \ P i P e C_{\eta} P^{\circ} P \ P_{\mu} P S P e P j P e \ C l^{\circ} P e P j P i C, P s P j P^{\circ} P j P e.$

$P_{\mu} P s P \pm C - C \dagger P S C - C_{\eta} P_{\mu} P^{\circ} P e C \dagger C - C -.$

$P \acute{K} P e P \ P_{\mu} C \dagger P_{\mu} \ P S P^{\circ} P i P_{\mu} P r P_{\mu} P S P s \ P i P_{\mu} C_{\eta} P_{\mu} P \gg C - P e \ P i P s P \pm C - C \dagger P S P e C \dots \ C_{\eta} P_{\mu} P^{\circ} P e C \dagger C - P N_{\epsilon},$
 $P i P e P \cdot P S P^{\circ} C \dagger P_{\mu} P S P e C \dots \ C r^{\circ} \ P i C_{\eta} P s C \dagger P_{\mu} C l^{\circ} C - \ P e P \gg C - P S C - C \dagger P S P e C \dots \ P r P s C l^{\circ} P \gg C - P r P \ P_{\mu} P S C_{\eta}$
 $P i C_{\eta} P e \ P \cdot P^{\circ} C l^{\circ} C, P s C l^{\circ} C r^{\circ} P i P^{\circ} P S P S C - \ P S C - P j P s P r P e P i C - P S C r^{\circ} \ P \cdot P^{\circ} \ P i P s P e P^{\circ} P \cdot P^{\circ} P S P S C l P j$
 $B \ll C l^{\circ} C r^{\circ} P \pm P^{\circ} C_{\eta} P^{\circ} C \dots P S P s C - P r P^{\circ} P \gg C_{\eta} P S P e P N_{\epsilon} \ P e C_{\eta} P s P i P s P i P e P \gg P e P i \ P i P S P^{\circ} C l^{\circ} P \gg C - P r P s P e$
 $C_{\eta} P s P \cdot C_{\eta} P e P i C r^{\circ} \ P^{\circ} P S P_{\mu} P i C_{\eta} P e P \cdot P j P e B \gg, \ C l l P e C - \ P \cdot P^{\circ} \ C \dagger P^{\circ} C l^{\circ} C, P s C, P s C_{\eta}$
 $C_{\eta} P s P \cdot P i P s P r C - P \gg P_{\mu} P S P s \ P \cdot P^{\circ} \ P S P^{\circ} C l^{\circ} C, C r^{\circ} P i P S P e P j P e \ P e P^{\circ} C, P_{\mu} P i P s C_{\eta} C - C l l P j P e: \ P r C r^{\circ} P \ P_{\mu}$
 $C \dagger P^{\circ} C l^{\circ} C, P s \ (\geq 1/10), \ C \dagger P^{\circ} C l^{\circ} C, P s \ (\geq 1/100, < 1/10), \ P S P_{\mu} C \dagger P^{\circ} C l^{\circ} C, P s \ (\geq 1/1000, \leq 1/100),$
 $C_{\eta} C - P r P e P s \ (\geq 1/10000, \leq 1/10000), \ P r C r^{\circ} P \ P_{\mu} \ C_{\eta} C - P r P e P s \ (< 1/10000), \ C \dagger P^{\circ} C l^{\circ} C, P s C, P^{\circ}$
 $P S P_{\mu} P i C - P r P s P j P^{\circ} \ (P S P_{\mu} P j P s P \ P \gg P e P i P s \ P i P e P \cdot P S P^{\circ} C \dagger P e C, P e \ P S P^{\circ} \ P s C l^{\circ} P S P s P i C -$
 $P S P^{\circ} C l l P i P S P e C \dots \ P r P^{\circ} P S P e C \dots).$

$P j \ P e P s P \ P_{\mu} P S C - P N_{\epsilon} \ P i C_{\eta} C r^{\circ} P i C - \ P \cdot P^{\circ} \ C \dagger P^{\circ} C l^{\circ} C, P s C, P s C_{\eta} \ P i P s P \pm C - C \dagger P S C - \ C_{\eta} P_{\mu} P^{\circ} P e C \dagger C - C -$
 $P i C_{\eta} P_{\mu} P r C l^{\circ} C, P^{\circ} P i P \gg P_{\mu} P S P s \ C r^{\circ} \ P i P s C_{\eta} C l l P r P e C r^{\circ} \ P \cdot P j P_{\mu} P S C \epsilon P_{\mu} P S P S C l l$
 $C l^{\circ} P_{\mu} C_{\eta} P N_{\epsilon} P s P \cdot P S P s C l^{\circ} C, C -.$

$P - \ P \pm P s P e C \acute{z} \ P e C_{\eta} P s P i C - \ C, P^{\circ} \ P \gg C - P j C, P^{\circ} C, P e C \dagger P S P s C - \ C l^{\circ} P e C l^{\circ} C, P_{\mu} P j P e: \ P S P_{\mu} C \dagger P^{\circ} C l^{\circ} C, P s \ B_{\eta}^{\circ}$
 $C, C_{\eta} P s P j P \pm P s C \dagger P e C, P s P i P_{\mu} P S C - C l l.$

$P - \ P \pm P s P e C \acute{z} \ C - P j C \acute{z} P S P S P s C - \ C l^{\circ} P e C l^{\circ} C, P_{\mu} P j P e: \ P S P_{\mu} C \dagger P^{\circ} C l^{\circ} C, P s \ B_{\eta}^{\circ} \ P^{\circ} P \gg P_{\mu} C_{\eta} P i C - C \dagger P S P^{\circ}$
 $C_{\eta} P_{\mu} P^{\circ} P e C \dagger C - C l l, \ P i P e C l^{\circ} P e P i P^{\circ} P S P S C l l.$

$P - \ P \pm P s P e C \acute{z} \ P S P_{\mu} C_{\eta} P i P s P i P s C - \ C l^{\circ} P e C l^{\circ} C, P_{\mu} P j P e: \ P S P_{\mu} C \dagger P^{\circ} C l^{\circ} C, P s \ B_{\eta}^{\circ} \ P i P s P \gg P s P i P S P e P N_{\epsilon}$
 $P \pm C - P \gg C_{\eta}.$

$P - \ P \pm P s P e C \acute{z} \ C l^{\circ} P_{\mu} C_{\eta} C \dagger C l l: \ P S P_{\mu} C \dagger P^{\circ} C l^{\circ} C, P s \ B_{\eta}^{\circ} \ C, P^{\circ} C \dots C - P e P^{\circ} C_{\eta} P r C - C l l; \ C_{\eta} C - P r P e P s \ B_{\eta}^{\circ}$
 $P \pm C_{\eta} P^{\circ} P r P e P e P^{\circ} C_{\eta} P r C - C l l.$

$P - \ P \pm P s P e C \acute{z} \ C l^{\circ} C \acute{z} P r P e P S P S P s C - \ C l^{\circ} P e C l^{\circ} C, P_{\mu} P j P e: \ P S P_{\mu} C \dagger P^{\circ} C l^{\circ} C, P s \ B_{\eta}^{\circ}$
 $P^{\circ} C_{\eta} C, P_{\mu} C_{\eta} C - P^{\circ} P \gg C_{\eta} P S P^{\circ} \ P i C - P i P s C, P_{\mu} P S P \cdot C - C l l, \ P i P^{\circ} P \cdot P s P r P e P \gg P^{\circ} C, P^{\circ} C \dagger C - C l l.$

$P - \ P \pm P s P e C \acute{z} \ C, C_{\eta} P^{\circ} P i P S P s C - \ C l^{\circ} P e C l^{\circ} C, P_{\mu} P j P e: \ P S P_{\mu} C \dagger P^{\circ} C l^{\circ} C, P s \ B_{\eta}^{\circ} \ P S C r^{\circ} P r P s C, P^{\circ};$
 $C_{\eta} C - P r P e P s \ B_{\eta}^{\circ} \ P e P e C \epsilon P e P s P i P^{\circ} \ P S P_{\mu} P i C_{\eta} P s C \dots C - P r P S C - C l^{\circ} C, C_{\eta}.$

$P - \ P \pm P s P e C \acute{z} \ P i P_{\mu} P i P^{\circ} C, P s P \pm C - P \gg C - P^{\circ} C_{\eta} P S P s C - \ C l^{\circ} P e C l^{\circ} C, P_{\mu} P j P e: \ C_{\eta} C - P r P e P s \ B_{\eta}^{\circ}$
 $C, C_{\eta} P^{\circ} P S P \cdot P e C, P s C_{\eta} P S P_{\mu} \ P i C - P r P i P e C \% P_{\mu} P S P S C l l \ P^{\circ} P e C, P e P i P S P s C l^{\circ} C, C -$
 $C, P_{\mu} C_{\eta} P j P_{\mu} P S C, C - P i \ P i P_{\mu} C \dagger C - P S P e P e.$

$P - \ P \pm P s P e C \acute{z} \ P s C_{\eta} P i P^{\circ} P S C - P i \ P r P e C \dots P^{\circ} P S P S C l l, \ P i C_{\eta} C \acute{z} P r P S P s C - \ P e P \gg C - C, P e P e \ C, P^{\circ}$
 $C l^{\circ} P_{\mu} C_{\eta} P_{\mu} P r P s C l^{\circ} C, C - P S P S C l l: \ P S P_{\mu} P i C - P r P s P j P s \ B_{\eta}^{\circ} \ P i C - P i P s P e C l^{\circ} C - C l l.$

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.