

Р†РќРŸРŸР РЈРЉРІР†РІ

**РrР»CП РjРµРrРёC‡PSPsPiPs Р·Р°CГC,PsCГCfPIP°PSPSCП Р»C-РёР°CГCГЧРёРёPsPiPs
Р·Р°CГPsP±CГ**

Р'РЈР"Р·РќРћР»РћР·Р¬РЉ

(BUDENOFALK^{В®})

РŸРёР»Р°Рr:

РrC-CHC‡Р°B CГРµC‡PsPIPёPSP°: Р±CГРrРµCГPsPSC-Рr;

1 C,PIPµCГРrР° РёР°РёCГCГP»Р° Р· РёРёCёРёPsPIPsCГPsP·C‡РёPSPSPёРjРё PiCГР°PSCГP»Р°РjРё
РjC-CГC,РёC,Ч 3 РjPi Р±CГРrРµCГPsPSC-РrCГ;B

*РrPsPiPsPjC-РПPSC- CГРµC‡PsPIPёPSPё: CГCГРёCГPsPIC- РёCГP»ЧРёРё, Р»Р°РёC,PsP·Рё
РjPsPSPsPiC-РrCГР°C,, PiPsPIC-РrPsPS РЉ 25, РjРµC,Р°РёCГРёP»PsPIPsC— РёРёCГP»PsC,Рё
РjРµC,РёP»РjРµC,Р°РёCГРёP»Р°C,CГ РёPsPiPsP»C-РjРµCГ (1 : 1) [PSP°PiCГРёРёР»Р°Рr
Р·CГРrCГР°PiC-C, L], РjРµC,Р°РёCГРёP»PsPIPsC— РёРёCГP»PsC,Рё
РjРµC,РёP»РjРµC,Р°РёCГРёP»Р°C,CГ РёPsPiPsP»C-РjРµCГ (1 : 2) [PSP°PiCГРёРёР»Р°Рr
Р·CГРrCГР°PiC-C, S], РёPsPiPsP»C-РjРµCГ РjРµC,Р°РёCГРёP»Р°C,CГ Р°РjPsPSC-Ч C,РёPi Р'
[PSP°PiCГРёРёР»Р°Рr Р·CГРrCГР°PiC-C, RS], РёPsPiPsP»C-РjРµCГ РjРµC,Р°РёCГРёP»Р°C,CГ
Р°РjPsPSC-Ч C,РёPi Рћ [PSP°PiCГРёРёР»Р°Рr Р·CГРrCГР°PiC-C, RL],B
C,CГРёРµC,РёP»C‡РёC,CГР°C,, C,Р°P»ЧРёРё, PsP±PsP»PsSPР° РёР°РёCГCзP»Рё:
РПРµP»Р°C,РёPS, C,РёC,Р°PSCГ РrC-PsРёCГРёРr (Р· 171), РµCГРёC,CГPsP·РёPS (Р· 127),B
Р·Р°P»C-Р·Р° PsРёCГРёРr C‡РµCГPIPsPSPёРµ (Р· 172), Р·Р°P»C-Р·Р° PsРёCГРёРrB
C‡PsCГPSPёРµ (Р· 172),B PSP°C,CГC-Ч Р»Р°CГРёРёP»CГCГP»ЧРёC,,Р°C,,.*

Р·C-РёР°CГCГЧРёРёР° C,,PsCГРjР°. РŸPIPµCГРrC-B РёР°РёCГCГP»Рё Р·
РёРёCёРёPsPIPsCГPsP·C‡РёPSPSPёРjРё PiCГР°PSCГP»Р°РjРё.

РћCГPSPsPIPsC- C,,C-Р·РёРёPs-C...C-РjC-C‡PSC- PIP»Р°CГC,РёPIPsCГC,C-:

*CГPsPПРµPIC- РёР°РёCГCГP»Рё (CГPsP·РjC-Ч 1), C%Ps РjC-CГC,CПC,Ч Р±C-Р»C-
РёCГCГPiP»C- PiCГР°PSCГP»Рё.B B B B*

Р»Р°CГРjР°РёPsC,РµCГР°РiРµPIC,РёC‡PSP° PiCГCГРiР°. РµCГPsC,РёР·Р°РiР°P»ЧРёPSC-
Р·Р°CГPsP±Рё, C%Ps Р·Р°CГC,PsCГPsPICГЧC,ЧCГCП PiCГРё
Р·Р°C...PIPsCГЧPIP°PSPSCПC... РёРёCёРµРµC‡PSPёРёCГ. РЉPsCГC,РёРёPsCГC,РµCГPsC—РrРё
РjC-CГC‡РµPIPsC— РrC-C—. РЉPsРr РћРŸX Рћ07Р· Рћ06.

Р»Р°CГРjР°РёPsP»PsPiC-C‡PSC- PIP»Р°CГC,РёPIPsCГC,C-.

PαP°CḡPjP°PePsPrPëPSP°PjC-PeP°.

PŷPsC‡PSPëPNē PjPμC...P°PSC-P·Pj PrC-C— P±CřPrPμCĠPsPSC-PrCř PiCḡPë
P»C-PeCřPIP°PSPSC- C...PIPsCḡPsP±Pë PḡCḡPsPSP° PSPμ P·ḡḡ™ CĠCĠPsPIP°PSPëPNē. P''P°PSC-
PeP»C-PSC-PePs-C,,P°CḡPjP°PePsP»PsPiC-C‡PSPsPiPs PrPsCĠP»C-PrPḡPμPSPSCĠ C,P°
C-PSCëPëC... PePsPSC,CḡPsP»CHPsPIP°PSPëC... PeP»C-PSC-C‡PSPëC...
PrPsCĠP»C-PrPḡPμPSCḡ C‡C-C,PePs CĠPIC-PrC‡P°C,CH, C%Ps PjPμC...P°PSC-P·Pj PrC-C—
P±CřPrPμCĠPsPSC-PrCř P±P°P·CřC''C,CHCĠCĠ P·PrPμP±C-P»CHCëPsPiPs PSP°
PjC-CĠC‡PμPIC-PNē PrC-C— PI PePëCëPμC‡PSPëPeCř. P'CřPrPμCĠPsPSC-Pr C''
PiP»CḡPePsPePsCḡC,PëPePsC—PrPsPj P· PIPëCĠPsPePsCḡ P»PsPeP°P»CHPSPsCḡ
PiCḡPsC,PëP·P°PiP°P»CHPSPsCḡ PrC-C''Cḡ. P' PrPsP·P°C..., PeP»C-PSC-C‡PSPs
PμPePIC-PIP°P»PμPSC,PSPëC... PrPsP·P°Pj CĠPëCĠC,PμPjPSPëC...
PiP»CḡPePsPePsCḡC,PëPePsC—PrC-PI, P±CřPrPμCĠPsPSC-Pr CĠPiCḡPëC‡PëPSCĠC''
P·PSP°C‡PSPs PjPμPSCëPμ PiCḡPëPiPSC-C‡PμPSPSCĠ PiC-PiPsC,P°P»P°PjPs-
PiC-PiPsC,,C-P·P°CḡPSPs-PSP°PrPSPëCḡPePsIPsP·P°P»PsP·PSPsC— CĠPëCĠC,PμPjPë C- PjP°C''
PjPμPSCëPëPNē PIPiP»PëPI PSP° PjP°CḡPePμCḡPë P·P°PiP°P»PμPSPSCĠ.

P'CřPrPμPSPsC,,P°P»CHPe PIPëCĠPIP»CĠC'' PrPsP·PsP·P°P»PμPḡPSPëPNē PIPiP»PëPI PSP°
CḡC-PIPμPSCḡ PePsCḡC,PëP·PsP»Cř Cř PiP»P°P·PjC-, CĠPePëPNē PiCḡPë
CḡPμPePsPjPμPSPPrPsPIP°PSC-PNē PrPsP·C- 3 × 3 PjPi P±CřPrPμCĠPsPSC-PrCř/PrPμPSCḡ C'',
P·PSP°C‡PSPs PSPëPḡC‡PëPj, PSC-Pḡ CḡC-PIPSsPμC,,PμPeC,PëPIPSC- PrPsP·Pë
CĠPëCĠC,PμPjPSPëC... PiP»CḡPePsPePsCḡC,PëPePsC—PrC-PI.

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

PḡP»C-PSC-C‡PSPμ PrPsCĠP»C-PrPḡPμPSPSCĠ Cē PiP°C‡C-C''PSC,C-PI P· C...PIPsCḡPsP±PsCḡ
PḡCḡPsPSP°

Pj CḡP°PSPPrPsPjC-P·PsPIP°PSPsPjCř, PiPsPrPIC-PNēPSPsPjCř CĠP»C-PiPsPjCř, P·
PiPsPrPIC-PNēPSPsCḡ C-PjC-C,P°C‡C-C''Cḡ PrPsCĠP»C-PrPḡPμPSPSC- Cř C...PIPsCḡPëC... P·
C...PIPsCḡPsP±PsCḡ PḡCḡPsPSP° PIC-Pr P»PμPiPePsPiPs PrPs PiPsPjC-CḡPSPsPiPs
CĠC,CřPiPμPSCĠ (200 < CDAI < 400), C-P· PIPiP»PëPIPsPj PSP° C,PμCḡPjC-PSP°P»CHPSPëPNē
PIC-PrPrC-P» PeP»CřP±PsPIPsC— PePëCëPePë C,P°/P°P±Ps PIPëCĠC...C-PrPSPsC— PePëCëPePë,
PμC,,PμPeC,PëPIPSC-CĠC,CH 9 PjPi P±CřPrPμCĠPsPSC-PrCř Cř PIPëPiP»CĠPrC- PsPrPSC-C''C—
PrPsP±PsPIPsC— PrPsP·Pë (9 PjPi OD) PiPsCḡC-PIPSCḡPIP°P»Pë P· P»C-PeCřPIP°PSPSCĠPj
P±CřPrPμCĠPsPSC-PrPsPj Cř PrPsP·C- 3 PjPi C,CḡPë CḡP°P·Pë PSP° PrPμPSCḡ (3 PjPi TID).

PμPμCḡPIPëPSPSPsCḡ PeC-PSC‡PμPIPsCḡ C,PsC‡PePsCḡ PμC,,PμPeC,PëPIPSPsCĠC,C- P±CřP»P°
C‡P°CĠC,PeP° PiP°C‡C-C''PSC,C-PI Cř CḡPμPjC-CĠC-C— (CDAI < 150) PSP° 8-PjCř C,PëPḡPSC-.

P'CĠCHPsPiPs 471 PiP°C‡C-C''PSC,C-PI P±CřP»Pë PIPeP»CḡC‡PμPSC- PI
PrPsCĠP»C-PrPḡPμPSPSCĠ (PiPsPIPSPëPNē PSP°P±C-Cḡ P°PSP°P»C-P·Cř, PαPhPŷ), 439
PiP°C‡C-C''PSC,C-PI P±CřP»Pë PIC-PrPiPsPIC-PrPSPs PrPs PiCḡPsC,PsPePsP»Cř (P P)
PSP°P±PsCḡCř P°PSP°P»C-P·Cř. PŷP°Pj PSPμ P±CřP»Ps PḡPsPrPSPëC... P·PSP°C‡PëPjPëC...
CḡPsP·C...PsPrPḡPμPSCḡ Cř PIPëC...C-PrPSPëC... C...P°CḡP°PeC,PμCḡPëCĠC,PëPeP°C...
PsP±PsC... PiCḡCřPi P»C-PeCřPIP°PSPSCĠ. Pj PiC-PrC,PIPμCḡPrPḡPμPSPSCĠ P°PSP°P»C-P·Cř,
71,3% PiP°C‡C-C''PSC,C-PI P±CřP»Pë PI CḡPμPjC-CĠC-C— PI 9 PjPi OD PiCḡCřPiPë C- 75,1% PI
3 PjPi TID PiCḡCřPiPë (PμPμ)B (P : 0,01975), C%Ps PrPμPjPsPSCĠC,CḡCřPIP°P»Pë PSPμ
PjPμPSCëCř PμC,,PμPeC,PëPIPSC-CĠC,CH 9 PjPi P±CřPrPμCĠPsPSC-PrCř OD PiPs
PIC-PrPSPsCëPμPSPSCḡ PrPs 3 PjPi P±CřPrPμCĠPsPSC-PrCř TID.

PkPμ PiPsPIC-PrPsPjP»CĠP»PsCĠCĠ PiCḡPs CĠPμCḡPNēPsP·PSC- PiPsP±C-C‡PSC- PμC,,PμPeC,Pë

РiPsPI'CIIP·P°PSC- P· PиCђPёPNёPsPjPsPj PиCђPµPиP°CђP°C,Cр.

PћC-PeCђPsCђPePsPиC-CђPSPёPNё PePsP»C-C.

PлP»C-PSC-CђPSC- PrPsCђP»C-PrP¶PµPSPSCII C-PSPrCзPeCђC-C— CђPµPjC-CђC-C— PиCђPё PePsP»P°PиPµPSPsPIPsPjCз PePsP»C-C,C-

P·C,,PµPeC,PёPIPSC-CђC,CH C,P° P±PµP·PиPµPeCр P·P°CђC,PsCђCрPIP°PSPSCII P±CрPrPµCђPsPSC-PrCр PrP»CII C-PSPrCрPeCђC-C— CђPµPjC-CђC-C— PиCђPё PePsP»P°PиPµPSPsPIPsPjCр PePsP»C-C,C- PsCђC-PSCђPIP°P»Pё Cр PrPIPsC... PиCђPsCђPиPµPeC,PёPIPSPёC... PиPsPrPIC-PNёPSPs CђP»C-PиPёC... (PµPђ), CђP°PSPrPsPjC-P·PsPIP°PSPёC..., PиP»P°CђPµP±Ps-PePsPSC,CђPsP»CHPsPIP°PSPёC..., P±P°PиP°C,PsCђPµPSC,CђPsPIPёC... PrPsCђP»C-PrP¶PµPSPSCII... P·P° CрCђP°CђC,CH PиP°CђC-C°PSC,C-PI P· P°PeC,PёPIPSPёPj PePsP»P°PиPµPSPsPIPёPj PePsP»C-C,PsPj.

P' PsPrPSPsPjCр PrPsCђP»C-PrP¶PµPSPSC- 30 PиP°CђC-C°PSC,C-PI P±CрP»Pё CђP°PSPrPsPjC-P·PsPIP°PSC- PrP»CII PsC,CђPёPjP°PSPSCII 9 PjPi P±CрPrPµCђPsPSC-PrCр PSP° PrPsP±Cр, 25 PиP°CђC-C°PSC,C-PI бђ" PrP»CII PsC,CђPёPjP°PSPSCII 3 Pi PjPµCђP°P»P°P·PёPSCр PSP° PrPsP±Cр, P° 37 PиP°CђC-C°PSC,C-PI бђ" PrP»CII PsC,CђPёPjP°PSPSCII PиP»P°CђPµP±Ps. PµPµCђPIPёPSPSPsCH P·PjC-PSPSPsCH PµC,,PµPeC,PёPIPSPsCђC,C- P±CрP»P° PeC-P»CHPeC-CђC,CH PиP°CђC-C°PSC,C-PI Cр CђC,р°PSC- PeP»C-PSC-CђPSPsC— CђPµPjC-CђC-C—, CIIPe° PIPёP·PSP°CђP°P»P°CђCII CIIPe ≤ 3 PIPёPиPsCђPsP¶PSPµPSPSCII PSP° PrPsP±Cр. 80 % PиP°CђC-C°PSC,C-PI, CIIPeC- PsC,CђPёPjCрPIP°P»Pё P±CрPrPµCђPsPSC-Pr, 44 % PиP°CђC-C°PSC,C-PI, CIIPeC- PsC,CђPёPjCрPIP°P»Pё PjPµCђP°P»P°P·PёPS, C- 59,5 % PиP°CђC-C°PSC,C-PI PиCђCрPиPё PиP»P°CђPµP±Ps PrPsCђCIIPiP»Pё PиPµCђPIPёPSPSPsC— PeC-PSCђPµPIPsC— C,PsCђPePё (P±CрPrPµCђPsPSC-Pr PиCђPsC,Pё PиP»P°CђPµP±Ps бђ" 0,072). P—PiC-PrPSPs P· C-PSCёPёPj PIPёP·PSP°CђPµPSPSCII Pj PeP»C-PSC-CђPSPsC— CђPµPjC-CђC-C—, C°Ps PICђP°C...PsPICрC" C,P°PePsP¶ PePsPSCђPёCђC,PµPSCђC-CH PIPёPиPsCђPsP¶PSPµPSCђ, C,PsP±C,Ps PI CђPµCђPµPrPSCђPsPjCр < 3 PIPёPиPsCђPsP¶PSPµPSCђ PSP° PrPsP±Cр C- PI CђPµCђPµPrPSCђPsPjCр < 1 PIPsPrCII PSPёCђC,PsPiPs PIPёPиPsCђPsP¶PSPµPSPSCII PSP° PrPsP±Cр PиCђPsC,CIIPiPsPj PsCђC,P°PSPSC-C... 7 PrPSC-PI PиPµCђPµPr PsCђC,P°PSPSC-Pj PиCђPёPNёPsPjPsPj PrPsCђP»C-PrP¶CрPIP°PSPsPiPs PиCђPµPиP°CђP°C,Cр, 80 % PиP°CђC-C°PSC,C-PI Cр PиCђCрPиC- P±CрPrPµCђPsPSC-PrCр, 32,0 % PиP°CђC-C°PSC,C-PI Cр PиCђCрPиC- PjPµCђP°P»P°P·PёPSCр C- 37,8 % PиP°CђC-C°PSC,C-PI Cр PиCђCрPиC- PиP»P°CђPµP±Ps PrPsCђCIIPiP»Pё CђPµPjC-CђC-C— (P±CрPrPµCђPsPSC-Pr Cр PиPsCђC-PIPSCII PSPSC- P· PиP»P°CђPµP±Ps: Cђ < 0,0006). P'CрPrPµCђPsPSC-Pr P±CрPI P±PµP·PиPµCђPSPёPj C- PrPsP±CђPµ PиPµCђPµPSPsCђPёPICђCII. P-PsPrPSPµ P· PSPµP±P°P¶P°PSPёC... CIIPIPёC° Cр PиCђCрPиC- P±CрPrPµCђPsPSC-PrCр PSPµ P±CрP»Ps PиPsPIбђ™ CIIP·P°PSPµ P· PиCђPёPNёPsPjPsPj PиCђPµPиP°CђP°C,Cр.

P' C-PSCёPsPjCр PrPsCђP»C-PrP¶PµPSPSC- 14 PиP°CђC-C°PSC,C-PI P±CрP»Pё CђP°PSPrPsPjC-P·PsPIP°PSC- PI PиCђCрPиCр P·P°CђC,PsCђCрPIP°PSPSCII 9 PjPi P±CрPrPµCђPsPSC-PrCр PSP° PrPsP±Cр, P° 14 бђ" PI PиCђCрPиCр P·P°CђC,PsCђCрPIP°PSPSCII PиP»P°CђPµP±Ps. PµPµCђPIPёPSPSPsCH P·PjC-PSPSPsCH PµC,,PµPeC,PёPIPSPsCђC,C- P±CрP»P° PeP»C-PSC-CђPSP° PIC-PrPiPsPIC-PrCH, CIIPe° PIPёP·PSP°CђP°P»P°CђCII CIIPe P·PSPёP¶PµPSPSCII PrPs ≤ 50 % P°PeC,PёPIPSPsCђC,C- P·P°C...PIPsCђCHPIP°PSPSCII PSP° PиPsCђP°C,PePsPIPsPjCр CђC-PIPSC-, P° PeP»C-PSC-CђPSP° P°PeC,PёPIPSC-CђC,CH P·P°C...PIPsCђCHPIP°PSPSCII PIPёP·PSP°CђP°P»P°CђCII CIIPe PeC-P»CHPeC-CђC,CH PIPёPиPsCђPsP¶PSPµPSCђ PиCђPsC,CIIPiPsPj PsCђC,P°PSPSC-C... 7 PrPSC-PI. 57,1 % PиP°CђC-C°PSC,C-PI Cр PиCђCрPиC- P±CрPrPµCђPsPSC-PrCр C,P° 21,4 % Cр PиCђCрPиC- PиP»P°CђPµP±Ps PrPsCђCIIPiP»Pё PeP»C-PSC-CђPSPsC— PIC-PrPiPsPIC-PrC- (Cђ = 0,05).

P'CrPrPμCfPSPSC-Pr P±CrPI P±PμP·PīPμC±PSPēPj C- PrPsP±CfPμ PīPμCfPμPSPsCfPēPICfCf. PJ PiCfCfPīC- P±CrPrPμCfPSPSC-PrCr PSPμ CfPīPsCfC,PμCfC-PiP°P»PsCfCf P¶PsPrPSPēC... CfPμCfPNēPsP·PSPēC... PīPsP±C-C±PSPēC... CfPμP°PeC†C-PNē.

PлP»C-PSC-C±PSPμ PrPsCfP»C-PrP¶PμPSPSCf P· PīC-PrC,CfPēPjP°PSPSCf CfPμPjC-CfC-C— PīCfPē PePsP»P°PiPμPSPsPIPsPjCé PePsP»C-C,C-

PлP»C-PSC-C±PSCf PμC,,PμPeC,PēPIPSC-CfC,Ch C,P° P±PμP·PīPμPeCf P·P°CfC,PsCfCfPīP°PSPSCf P±CrPrPμCfPSPSC-PrCr PrP»Cf PīC-PrC,CfPēPjP°PSPSCf CfPμPjC-CfC-C— PīCfPē PePsP»P°PiPμPSPsPIPsPjCf PePsP»C-C,C- PsC†C-PSCfPīP°P»Pē Cr PīCfPSCfPīPμPeC,PēPIPSPsPjCf PīPsPrPIC-PNēPSPs CfP»C-PīPsPjCf (PμPŸ), CfP°PSPPrPsPjC-P·PsPīP°PSPsPjCf, PīP»P°C†PμP±Ps-PePsPSC,CfPsP»ChPsPīP°PSPsPjCf, P±P°PiP°C,PsC†PμPSC,CfPsPIPsPjCf PrPsCfP»C-PrP¶PμPSPSC- P·P° CrC†P°CfC,Ch PīP°C†C-C"PSC,C-PI P· PePsP»P°PiPμPSPsPIPēPj PePsP»C-C,PsPj Cr CfC,P°PrC-C— CfPīPsPePsCh.

PμPμCfPIPēPSPSPsCh PeC-PSC†PμPIPsCh C,PsC†PePsCh P±CrP»P° C†P°CfC,PeP° PīP°C†C-C"PSC,C-PI P· PeP»C-PSC-C±PSPsCh CfPμPjC-CfC-C"Ch PīCfPsC,CfPiPsPj 52 C,PēP¶PSC-PI. P PμPjC-CfC-Cf PIPēP·PSP°C†P°P»P°CfCf CfPe CfPμCfPμPrPSC-PNē PīPsPeP°P·PSPēPe < 3 PIPēPīPsCfPsP¶PSPμPSCf PSP° PrPsP±Cr, P· CfPePēC... CfPμCfPμPrPSC-PNē PīPsPeP°P·PSPēPe < 1 PIPsPrCfPSPēCfC,PsPiPs PIPēPīPsCfPsP¶PSPμPSPSCf PSP° PrPsP±Cr, PīCfPsC,CfPiPsPj C,PēP¶PSCf PīPμCfPμPr PsCfC,P°PSPSC-Pj PIC-P·PēC,PsPj C- PIC-PrCfCfC,PSC-CfC,Ch CfPμC†PēPrPēPICf PīCfPsC,CfPiPsPj 1 CfPsPeCf. P PμC†PēPrPēPI PIPēP·PSP°C†P°PICfCf CfPe CfPμCfPμPrPSC-PNē PīPsPeP°P·PSPēPe ≥ 3 PIPēPīPsCfPsP¶PSPμPSCf PSP° PrPsP±Cr, P· PSPēC... ≥ 1 PIPsPrCfPSPēCfC,PsPiPs PIPēPīPsCfPsP¶PSPμPSPSCf PSP° PrPsP±Cr, PīCfPsC,CfPiPsPj PīPsPīPμCfPμPrPSCfPsPiPs C,PēP¶PSCf.

92 PīP°C†C-C"PSC,Pē P±CrP»Pē CfP°PSPPrPsPjC-P·PsPīP°PSC- PrP»Cf P»C-PeCfPīP°PSPSCf Cr C,,P°P·C- PμPŸ (44 PīP°C†C-C"PSC,Pē PsC,CfPēPjCfPīP°P»Pē P±CrPrPμCfPSPSC-Pr, 48 бf" PīP»P°C†PμP±Ps) C- PīCfPēPNēPSCfP»Pē PīCfPēPSP°PNēPjPSC- PsPrPSCf PrPsP·Cr PrPsCfP»C-PrP¶CfPīP°PSPsPiPs PīCfPμPīP°CfP°C,Cf (PīPsPīPSP° PIPēP±C-CfPeP° P°PSP°P»C-P·Cr, FAS). PμPsP·PsP»PsPiC-Cf CfC,P°PSPsPIPēP»P° 6 PjPi P±CrPrPμCfPSPSC-PrCr/PrPsP±Cr, C%Ps C†PμCfPiCfPīP°P»PēCfCf P· 3 PjPi P±CrPrPμCfPSPSC-PrCr/PrPsP±Cr (C%Ps PIC-PrPīPsPIC-PrP°C" CfPμCfPμPrPSC-PNē PrPsP±PsPIC-PNē PrPsP·C- 4,5 PjPi P±CrPrPμCfPSPSC-PrCr). PJ PeC-PSC†PμPIPsPjCf P°PSP°P»C-P·C- P·PSP°C†PSPs P±C-P»ChCfPμ PīP°C†C-C"PSC,C-PI P· PiCfCfPīPē P±CrPrPμCfPSPSC-PrCr (61,4 %) PīPsCfC-PiPSCfPSPs P· PīP°C†C-C"PSC,P°PjPē P· PiCfCfPīPē PīP»P°C†PμP±Ps (16,7 %) PrPsCfCfPiP»Pē PīPμCfPIPēPSPSPsC— PeC-PSC†PμPIPsC— C,PsC†PePē, C%Ps CfPIC-PrC†PēC,Ch PīCfPs PīPμCfPμPīP°PiCf P±CrPrPμCfPSPSC-PrCr PSP°Pr PīP»P°C†PμP±Ps (Cf < 0,001).

PлP»C-PSC-C±PSPμ PrPsCfP»C-PrP¶PμPSPSCf C-PSPrCéPeC†C-C— CfPμPjC-CfC-C— PīCfPē P»C-PjC,,PsC†PēC,P°CfPSPsPjCé PePsP»C-C,C-

PлP»C-PSC-C±PSCf PμC,,PμPeC,PēPIPSC-CfC,Ch C,P° P±PμP·PīPμPeCf P·P°CfC,PsCfCfPīP°PSPSCf P±CrPrPμCfPSPSC-PrCr PrP»Cf C-PSPrCfPeC†C-C— CfPμPjC-CfC-C— P»C-PjC,,PsC†PēC,P°CfPSPsPiPs PePsP»C-C,Cf PsC†C-PSCfPīP°P»Pē Cr PīCfPSCfPīPμPeC,PēPIPSPsPjCf, PīPsPrPIC-PNēPSPs CfP»C-PīPsPjCf (PμPŸ), CfP°PSPPrPsPjC-P·PsPīP°PSPsPjCf, PīP»P°C†PμP±Ps-PePsPSC,CfPsP»ChPsPīP°PSPsPjCf, P±P°PiP°C,PsC†PμPSC,CfPsPIPsPjCf PrPsCfP»C-PrP¶PμPSPSC- P·P° CrC†P°CfC,Ch PīP°C†C-C"PSC,C-PI P· P°PeC,PēPIPSPēPj P»C-PjC,,PsC†PēC,P°CfPSPēPj PePsP»C-C,PsPj.

$$\text{P}\delta\text{Pu}\text{C}\eta\text{Pu}\cdot\text{C}\dot{\text{I}}\text{P}\dot{\text{i}}\text{Pu}\text{C}\dagger\text{P}\ddot{\text{e}}\text{C}_{,,}\text{C}-\text{C}\dagger\text{P}\text{SPu}\text{P}\ddot{\text{i}}\text{P}\text{S}\text{P}\text{e}\text{C}\eta\text{P}\ddot{\text{e}}\text{C}_{,,}\text{C}\text{C}\text{I}\text{C}\text{€P}\rangle\text{C}\dot{\text{r}}\text{P}\text{SP}\text{e}\text{P}\text{s}\text{P}\text{I}\text{P}\text{s}-\text{C}\dot{\text{I}}\text{C}_{,,}\text{C}-\text{P}\text{M}\text{P}\text{e}\text{P}\ddot{\text{e}}\text{C}...$$

PiC₇P°PSCrP» PiC₇PμPiP°C₇P°C, Cr P'CrPrPμPSPsC,,P°P»CHPe, C,PIPμC₇PrC- PeP°PiC₇CrP»Pë
 PiPs 3 PjPi, C-C₇PSCrC" P»P°Pi-C,,P°P·P° 2-3 PiPsPrPëPSPë. PμC-C₇P»C₇
 PsPrPSPsC₇P°P·PsPIPSPiPs PiC₇PëPNëPsPjCr PsPrPSC-C"C—
 PePëC€PePsPIPSC₇PsP·C±PëPSPSPsC— PeP°PiC₇CrP»Pë P'CrPrPμPSPsC,,P°P»CHPe 3 PjPi
 PiPμC₇PμPr C—P₇PμC₇, C₇PμC₇PμPrPSC-PNë PjP°PeC₇PëPjP°P»CHPSPëPNë C₇C-PIPμPSC₇
 P±C₇PrPμC₇PsPSC-PrCr PI PiP»P°P·PjC-, C%Ps C₇PeP»P°PrP°C" 1-2 PSPi / PjP»,
 C₇PiPsC₇C,PμC₇C-PiP°PIC₇C₇ Cr P·PrPsC₇PsPIPëC... PsC₇C-P± C- Cr PiP°C₇C-C"PSC,C-PI P·
 C...PIPSC₇PsP±PsC₇ P₇C₇PsPSP° PiC₇PëP±P»PëP·PSPs C±PμC₇PμP· 5 PiPsPrPëPS PiC-C₇P»C₇
 PiC₇PëPNëPsPjCr. P₇P°PeC₇PëPjP°P»CHPSPμ PIPëPIC-P»CHPSPμPSPSC₇ PiC₇PμPiP°C₇P°C, Cr
 C₇PiPsC₇C,PμC₇C-PiP°P»PsC₇C₇ PI C,PμC₇PjC-PSP°P»CHPSPëC... PIC-PrPrC-P»P°C...
 PeP»C₇P±PsPIPSC— C- C₇P»C-PiPsC— PePëC€C₇C-, PsC₇PSPsPIPSPëC... PrC-P»C₇PSPeP°C...
 P·P°PiP°P»PμPSPSC₇ PiC₇Pë C...PIPSC₇PsP±C- P₇C₇PsPSP°.

P₇PrPSPsC±P°C₇PSPμ C₇PiPsP₇PëPIP°PSPSC₇ C—P₇C- PjPsP₇Pμ P·P°C,C₇PëPjP°C,Pë
 PiC₇PsC...PsPrP₇PμPSPSC₇ PiC₇PμPiP°C₇P°C, Cr C±PμC₇PμP· C€P»C₇PSPePsPIPSC-
 PePëC€PePsPIPëPNë C,C₇P°PeC, PiC₇PëP±P»PëP·PSPs PSP° 2-3 PiPsPrPëPSPë. Pj C₇CHPsPjCr
 PIPëPiP°PrPeCr P·P°C,C₇PëPjPeP° PiPsPiP»PëPSP°PSPSC₇ C₇C,P°PSPsPIPëC,CH
 PiC₇PëP±P»PëP·PSPs 4-6 PiPsPrPëPS. PiPμ PSPμ PjP°C" PIPiP»PëPIC₇ PSP°
 C€PIPëPrPeC-C₇C,CH PiPsPiP»PëPSP°PSPSC₇.

P PsP·PiPsPrC-P»

P'CrPrPμC₇PsPSC-Pr PjP°C" PIPëC₇PsPePëPNë PsP±B₇™C"Pj C₇PsP·PiPsPrC-P»Cr
 (P±P»PëP·CHPePs 3 P»/PePi). P—PiB₇™C₇P·C₇PIP°PSPSC₇ P· P±C-P»PeP°PjPë PiP»P°P·PjPë
 C₇C,P°PSPsPIPëC,CH 85–90 %.

P'C-PsC,C₇P°PSC₇C,,PsC₇PjP°C₇C-C₇

P'CrPrPμC₇PsPSC-Pr PiC-PrP»C₇PiP°C" C-PSC,PμPSC₇PëPIPSC-PNë
 P±C-PsC,C₇P°PSC₇C,,PsC₇PjP°C₇C-C— Cr PiPμC±C-PSC₇C- (P±P»PëP·CHPePs 90 %) PrPs
 PjPμC,P°P±PsP»C-C,C-PI P· PSPëP·CHPePsC₇
 PiP»C₇PePsPePsC₇C,PëPePsC₇C,PμC₇PsC—PrPSPsC₇ P°PeC,PëPIPSC-C₇C,C₇.
 P"P»C₇PePsPePsC₇C,PëPePsC₇C,PμC₇PsC—PrPSP° P°PeC,PëPIPSC-C₇C,CH PsC₇PSPsPIPSPëC...
 PjPμC,P°P±PsP»C-C,C-PI, 6β-PiC-PrC₇PsPeC₇PëP±C₇PrPμC₇PsPSC-PrCr C- 16α-
 PiC-PrC₇PsPeC₇PëPiC₇PμPrPSC-P·PsP»PsPSC₇, C₇PeC- CrC,PIPSC₇C₇C₇C,CHC₇C₇
 C±PμC₇PμP· CYP3A4, C₇C,P°PSPsPIPëC,CH PjPμPSC€Pμ 1 % C,P°PePsC—
 P±C₇PrPμC₇PsPSC-PrCr.

P'PëPIPμPrPμPSPSC₇

P₇PμC₇PμPrPSC-PNë PiPμC₇C-PsPr PSP°PiC-PIPIPëPIPμPrPμPSPSC₇ PiC-C₇P»C₇
 PiPμC₇PsC₇P°P»CHPSPsPiPs PiC₇PëPNëPsPjCr C₇C,P°PSPsPIPëC,CH P±P»PëP·CHPePs 3–4
 PiPsPrPëPS. P₇PëC₇C,PμPjPSP° PrPsC₇C,C₇PiPSC-C₇C,CH Cr P·PrPsC₇PsPIPëC...
 PrPsP±C₇PsPIPSP»CHC₇C-PI, P° C,P°PePsP₇ Cr PiP°C₇C-C"PSC,C-PI C-P·
 P·P°PiP°P»CHPSPëPjPë P·P°C...PIPSC₇C₇PIP°PSPSC₇PjPë PePëC€PμC±PSPëPeP°
 PSP°C,C%PμC₇PμC₇C₇Pμ C₇C,P°PSPsPIPëC,CH P±P»PëP·CHPePs 9–13 %. P₇P»C-C₇PμPSC₇
 P±C₇PrPμC₇PsPSC-PrCr C₇C,P°PSPsPIPëC,CH P±P»PëP·CHPePs 10–15 P»/C...PI. P»PëC€Pμ
 PSPμP·PSP°C±PSP° PeC-P»CHPeC-C₇C,CH P'CrPrPμC₇PsPSC-PrCr PIPëIPsPrPëC,CHC₇C₇
 PSPëC₇PeP°PjPë.

P₇PiPμC₇PëC,,C-C±PSC- PiC₇C±PiPë PiP°C₇C-C"PSC,C-PI (PiP°C₇C-C"PSC,Pë P·
 PiPsC₇C±C€PμPSPSC₇PjPë C,,C±PSPeC₇C-C— PiPμC±C-PSPePë)

C-PSC€C- PIPëPrPë PIP·P°C"PjPsPrC-PN.

PαP°CḤPjP°PePsPrPëPSP°PjC-CḥPSC- PIP·P°C"PjPsPrC-C—

- *PŸPμCḤC†PμPIC- PiP»C-PePsP·PëPrPë*

P"C-CḤ PiP»C-PePsP·PëPrC-PI PjPsP¶Pμ PīPsC,PμPSC†C-CḥPIP°C,PëC†CḤ PrPμC,,C-C†PëC,PsPj PeP°P»C-Cḥ.

B· *PŸP°P»CḥCḤPμC,PëPePë*

P·PeC†PeCḤPμC†C-CḤ PeP°P»C-Cḥ PjPsP¶Pμ PīPsC†PëP»CḥPIP°C,PëC†Cḥ.

PαP°CḤPjP°PePsPeC-PSPμC,PëCḥPSC- PIP·P°C"PjPsPrC-C—

B· *P†PëC,PsC...CḤPsPj P 450 3Pḥ (CYP3A4)*

P†PSPiC-P±C-C,PsCḤPë CYP3A4. PhC†C-PeC†C"C,ChC†CḤ, C%Ps PsPrPSPsC†P°C†PSPμ P»C-PeC†PIP°PSPSCḤ C-PSPiC-P±C-C,PsCḤP°PjPë CYP3A4, PIPeP»CḥC†P°CḥC†Pë PīCḤPμPīP°CḤP°C,Pë, C%Ps PjC-C†C,CḤC,Ch PePsP±C-C†PëC†C,P°C,, PīC-PrPIPëC%CrC" CḤPëP·PëPe PIPëPSPëPePSPμPSPSCḤ C†PëC†C,PμPjPSPëC... PīPsP±C-CḥPSPëC... PμC,,PμPeC,C-PI. PḥPsPjP±C-PSP°C†C-C— P±C†PrPμC†PsPSC-PrC† P· PePsP±C-C†PëC†C,P°C,PsPj C†P»C-Pr C†PSPëPeP°C,Pë, CḤPeC%Ps PePsCḤPëC†C,Ch PSPμ PīPμCḤPμPIPëC%CrC" CḤPëP·PëPe PIPëPSPëPePSPμPSPSCḤ C†PëC†C,PμPjPSPëC... PīPsP±C-CḥPSPëC... PμC,,PμPeC,C-PI PePsCḤC,PëPePsC†C,PμCḤPsC—PrC-PI. PJ PIPëPīP°PrPeC†, PePsP»Pë PePsCḤPëC†C,Ch PIC-Pr PīCḤPëPNḥPsPjC† P±C†PrPμC†PsPSC-PrC† PīPμCḤPμPIPëC%CrC" C,P°PePëPNḥ CḤPëP·PëPe, PīP°C†C-C"PSC,C-PI C†P»C-Pr PePsPSC,CḤPsP»CḥPIP°C,Pë C%PsPrPs PīPsCḤPIPë C†PëC†C,PμPjPSPëC... PīPsP±C-CḥPSPëC... PμC,,PμPeC,C-PI PePsCḤC,PëPePsC†C,PμCḤPsC—PrC-PI.

PμPμCḤPsCḤP°P»CḥPSPëPNḥ PīCḤPëPNḥPsPj PePμC,PsPePsPSP°P·PsP»C† 200 PjPi PsPrPëPS CḤP°P· PSP° PrPμPSCḥ P·P±C-P»CḥC€C†C" PePsPSC†PμPSC,CḤP°C†C-Cḥ P±C†PrPμC†PsPSC-PrC† (PsPrPSPsCḤP°P·PsPIP° PrPsP·P° 3 PjPi) PI PīP»P°P·PjC- PīCḤPëP±P»PëP·PSPs PI 6 CḤP°P·C-PI PīCḤPë PsPrPSPsC†P°C†PSPsPjC† P·P°C†C,PsC†C†PIP°PSPSC-. PμCḤPë PīCḤPëPNḥPsPjC- PePμC,PsPePsPSP°P·PsP»C† PīCḤPëP±P»PëP·PSPs C†PμCḤPμP· 12 PīPsPrPëPS PīC-C†P»CḤ P±C†PrPμC†PsPSC-PrC† PePsPSC†PμPSC,CḤP°C†C-CḤ PsC†C,P°PSPSCHPsPiPs P·P±C-P»CḥC€C†C"C,ChC†CḤ PīCḤPëP±P»PëP·PSPs PI 3 CḤP°P·Pë. PJ P·PIbḤ™ CḤP·PeC† P· PSPμPrPsC†C,P°C,PSC-C†C,Cḥ PrP°PSPëC... C%PsPrPs CḤPμPePsPjPμPSPPrPsPIP°PSPëC... PrPsP· C†P»C-Pr C†PSPëPeP°C,Pë C,P°PePsC— PePsPjP±C-PSP°C†C-C—.

P†PSC€C- PīPsC,C†P¶PSC- C-PSPiC-P±C-C,PsCḤPë CYP3A4, C,P°PeC- CḤPe CḤPëC,PsPSP°PIC-CḤ, C-C,CḤP°PePsPSP°P·PsP», PeP»P°CḤPëC,CḤPsPjC-C†PëPS C- PīCḤPμPNḥPīC,,CḤC†C,PsPIPëPNḥ C†C-Pe, C,P°PePsP¶ PjPsP¶C†C,Ch C†PīCḤPëC†PëPSPëC,Pë PīPsPjC-C,PSPμ P·P±C-P»CḥC€PμPSPSCḤ PīP»P°P·PjPsPIPsC— PePsPSC†PμPSC,CḤP°C†C-C— P±C†PrPμC†PsPSC-PrC†. PŸPsPjC† C†P»C-Pr C†PSPëPeP°C,Pë C—C... PsPrPSPsC†P°C†PSPsPiPs P·P°C†C,PsC†C†PIP°PSPSCḤ.

P†PSPrC†PeC,PsCḤPë CYP3A4, C,P°PeC- CḤPe PeP°CḤP±P°PjP°P·PμPīC-PS C- CḤPëPjC,,P°PīC-C†PëPS, PjPsP¶C†C,Ch P·PSPëP¶C†PIP°C,Pë CḤPe C†PëC†C,PμPjPSC†, C,P°Pe C- PjC-C†C†PμPIC† PrC-Cḥ P±C†PrPμC†PsPSC-PrC† PSP° C†P»PëP·PsPIC† PsP±PsP»PsPSPeC† PePëC€PμC†PSPëPeC†. P"PsP·C†PIP°PSPSCḤ P±C†PrPμC†PsPSC-PrC† PīPsC,CḤPμP±C†C" PePsCḤPëPīC†PIP°PSPSCḤ.

PiPsC, CḡPμP±CfCḡC, Cḡ PiP°C†C-C"PS C, Pē P· PsPrPSPēPj P°P±Ps PeC-P»CḡPePsPjP° P· C, P°PePēC... P·P°C...PIPsCḡCḡPIP°PSCḡ: C, C†P±PμCḡPeC†P»CḡPsP·, P°CḡC, PμCḡC-P°P»CḡPSP° PiC-PiPμCḡC, PμPSP·C-Cḡ, C†C†PeCḡPsPIPēPNē PrC-P°P±PμC,, PsC†C, PμPsPiPsCḡPsP·, PiPμPiC, PēC†PSP° PIPēCḡP°P·PeP° (CēP»C†PSPeP° P°P±Ps PrPIP°PSP°PrC†CḡC, PēPiP°P»PsC— PePēCēPePē), PiP»P°C†PePsPjP°, PeP°C, P°CḡP°PeC, P°, PIPēPiP°PrPePē PrC-P°P±PμC, C† P°P±Ps PiP»P°C†PePsPjPē PI C†C-PjPμPNēPSPsPjC† P°PSP°PjPSPμP·C- P°P±Ps P±C†PrCḡ-CḡPePēPNē C-PSCēPePNē C†C, P°PS, PiCḡPē CḡPePsPjC† PiP»CḡPePsPePsCḡC, PēPePsC†C, PμCḡPsC—PrPē PjPsPḡC†C, Cḡ PIPēCḡPIP»CḡC, Pē PSPμP±P°PḡP°PSC- PμC,, PμPeC, Pē.

PiPμPNē PiCḡPμPiP°CḡP°C, PSPμ PiC-PrC...PsPrPēC, Cḡ PiP°C†C-C"PS C, P°Pj, CḡPeC- C†C, CḡP°PḡPrP°CḡC, Cḡ PSP° C...PIPsCḡPsP±C† PḡCḡPsPSP° PIPμCḡC...PSC-C... PIC-PrPrC-P»C-PI CēP»C†PSPePsPIPs-PePēCēPePsPIPsPiPs C, CḡP°PeC, C†.

P— PsPiP»CḡPrC† PSP° PiPμCḡPμPIP°PḡPSPs PjC-C†C†PμPIC† PrC-Cḡ PiCḡPμPiP°CḡP°C, C† PSPμ PjPsPḡPSP° PsC†C-PeC†PIP°C, Pē C†PiCḡPēCḡC, P»PēPIPēC... PμC,, PμPeC, C-PI PrP»Cḡ PiP°C†C-C"PS C, C-PI P· PiPsP·P°PePēCēPePsPIPēPjPē C†PēPjPiC, PsPjP°PjPē (PSP°PiCḡPēPeP»P°Pr C, P°PePēPjPē, C%Ps PiCḡPsCḡPIP»CḡCḡC, CḡC†Cḡ PSP° CēPeC-CḡC-, PsC†P°C... P°P±Ps C†C†PiP»PsP±P°C...).

PḡPsPḡC†C, Cḡ PIPēPSPēPeP°C, Pē C†PēC†C, PμPjPSC- PμC,, PμPeC, Pē PePsCḡC, PēPePsC†C, PμCḡPsC—PrC-PI, PsC†PsP±P»PēPIPs C† CḡP°P·C- PiCḡPēP·PSP°C†PμPSPSCḡ PiCḡPμPiP°CḡP°C, C† C† PIPēC†PsPePēC... PrPsP·P°C... C- PiCḡPsC, CḡPiPsPj C, CḡPēPIP°P»PēC... PiPμCḡC-PsPrC-PI C†P°C†C†. PḡPsPrC-P±PSC- PμC,, PμPeC, Pē PjPsPḡC†C, Cḡ PIPeP»CḡC†P°C, Pē C†PēPSPrCḡPsPj PḡC†CēPēPSPiP°, PiCḡPēPiPSC-C†PμPSPSCḡ C,, C†PSPeC†C-C— PSP°PrPSPēCḡPePsPIPēC... P·P°P»PsP·, P·P°C, CḡPēPjPeC† CḡPsC†C, C†, P·PSPēPḡPμPSPSCḡ PjC-PSPμCḡP°P»CḡPSPsC— C%C-P»CḡPSPsC†C, C- PeC-C†C, PePsPIPsC— C, PeP°PSPēPSPē, PeP°C, P°CḡP°PeC, C†, PiP»P°C†PePsPjC† C- CēPēCḡPsPePēPNē C†PiPμPeC, Cḡ PiC†PēC...C-C†PSPēC.../PiPsPIPμPrC-PSPePsPIPēC... CḡPsP·P»P°PrC-PI (PrPēPI. C, P°PePsPḡ CḡPsP·PrC-P» B«PḡPsP±C-C†PSC- CḡPμP°PeC†C-C—B»).

P†PSC,, PμPeC†C-C—

PḡCḡPēPiPSC-C†PμPSPSCḡ CḡPμP°PeC†C-C—PIC-PrPiPsPIC-PrC- PSP° P·P°PiP°P»PμPSPSCḡ C- PiCḡPēPiPSC-C†PμPSPSCḡ C-PjC†PSPSPsC— C†PēC†C, PμPjPē PiC-PrPIPēC%C†C" C†PiCḡPēPNēPSCḡC, P»PēPIC-C†C, Cḡ PrPs C-PSC,, PμPeC†C-C— C, P° C, CḡPḡPeC-C†C, Cḡ C—C— PiCḡPsC, C-PeP°PSPSCḡ. PḡP»C-Pr CḡPμC, PμP»CḡPSPs PsC†C-PSPēC, Pē CḡPēP·PēPe PsP±C, CḡPḡPμPSPSCḡ P±P°PeC, PμCḡC-P°P»CḡPSPēC..., PiCḡPēP±PePsPIPēC..., P°PjPμP±PSPēC... C- PIC-CḡC†C†PSPēC... C-PSC,, PμPeC†C-PNē PSP° C, P»C- P»C-PeC†PIP°PSPSCḡ PiP»CḡPePsPePsCḡC, PēPePsC—PrP°PjPē. PḡP»C-PSC-C†PSC- PiCḡPsCḡPIPē PjPsPḡC†C, Cḡ P±C†C, Pē P°C, PēPiPsPIPēPjPē, C- C†PμCḡPNēPsP·PSC- C-PSC,, PμPeC†C-C—, C, P°PeC- CḡPe C†PμPiC†PēC† C- C, C†P±PμCḡPeC†P»CḡPsP·, PjPsPḡC†C, Cḡ PjP°C†PeC†PIP°C, PēC†Cḡ C- PrPsC†CḡPiP°C, Pē CḡPsP·PIPēPSC†C, PsC— C†C, P°PrC-C— PrPs C, PsPiPs, CḡPe PIPsPSPē P±C†PrC†C, Cḡ CḡPsP·PiC-P·PSP°PSC-.

P'C-C, CḡCḡPSP° PIC-C†PiP°

PḡP° PsC†PsP±P»PēPIC† C†PIP°PiC† P·P°C†P»C†PiPsPIC†C" PIC-C, CḡCḡPSP° PIC-C†PiP°, C, PsPjC† C%Ps C†Pμ P·P°C...PIPsCḡCḡPIP°PSPSCḡ PjPsPḡPμ P±C†C, Pē C, CḡPḡPePēPj, P°

C-PSPsPrC- C- P»PµC,P°P»CHbPSPëPj Cí PïP°C†C-C"psc,C-PI P· PïCḡPëPiPSC-C‡PµPSPëPj
C-PjCíPSC-C,PµC,PsPj. PµP°C†C-C"psc,Pë, CµPeC- PSPµ C...PIPsCḡC-P»Pë PSP° C†Pµ
P·P°C...PIPsCḡCḡPIP°PSPSCµ, PïPsPIPëPSPSC- CíPSPëPeP°C,Pë C,C-CḡPSPsPiPs
PïPµCḡCḡPsPSP°P»CHbPSPsPiPs PePsPSC,P°PeC,Cí P· C...PIPsCḡPëPjPë PSP° PIC-C,CḡCµPSCí
PIC-CḡPíCí P°P±Ps PsPïPµCḡC-P·CíCḡC‡PëPNë P»PëCëP°PNë (PiPµCḡPiPµCḡ P·PsCḡC,PµCḡ). Pj
CḡP°P·C- CµPeC%Ps C,P°PePëPNë PePsPSC,P°PeC, PIP¶Pµ PIPëPSPëPe, PïP°C†C-C"psc,Cí
CḡP»C-Pr P·PIPµCḡPSCíC,PëCḡCµ P·P° C,PµCḡPjC-PSPsPIPsCḡ
PePsPSCíCíP»CHbC,P°C†C-C"ḡ PrPs P»C-PeP°CḡCµ. PhPSP°P»PsPiC-C‡PSC-
CḡPµPePsPjPµPSPPrP°C†C-C— PïPsC,CḡC-P±PSPs PSP°PrP°C,Pë P±P°C,CHbPeP°Pj
PïP°C†C-C"psc,P°-PrPëC,PëPSPë. PkPµC-PjCíPSC-P·PsPIP°PSC- PïP°C†C-C"psc,Pë, CµPeC-
PïCḡPëPNëPjP°CḡC,CHb CḡPëCḡC,PµPjPSC- PePsCḡC,PëPePsCḡC,PµCḡPsC—PrPë P°P±Ps
PïCḡPëPNëPjP°P»Pë C—C... PïCḡPsC,CµPiPsPj PsCḡC,P°PSPSC-C... 3 PjC-CḡCµC†C-PI,
PïC-CḡP»Cµ PePsPSC,P°PeC,Cí P· C...PIPsCḡPëPj PSP° PsPïPµCḡC-P·CíCḡC‡PëPNë PiPµCḡPiPµCḡ
PïPsC,CḡPµP±CíCḡC,CHb PïP°CḡPëPIPSPsC— C-PjCíPSC-P·P°C†C-C—
C-PjCíPSPsPiP»PsP±CíP»C-PSPsPj PrPs PIC-CḡCíCḡCí PsPïPµCḡC-P·CíCḡC‡PsPiPs
PiPµCḡPiPµCḡCí. PµP°CḡPëPIPSCí C-PjCíPSC-P·P°C†C-Cḡ PïPsC,CḡC-P±PSPs
PïCḡPsPIPµCḡC,Pë PIPïCḡPsPrPsPIP¶ 10 PrPSC-PI PïC-CḡP»Cµ PePsPSC,P°PeC,Cí P·
PIC-C,CḡCµPSPsCḡ PIC-CḡPïPsCḡ. PïPeC%Ps PIC-C,CḡCµPSP° PIC-CḡPïP° P±CíP»P°
PïC-PrC,PIPµCḡPrP¶PµPSP°, C...PIPsCḡPsP±P° PIPëPjP°PiP°C" PSPµPiP°PNëPSPsPiPs
CḡPiPµC†C-P°P»CHbPSPsPiPs P»C-PeCíPIP°PSPSCµ.

PµCḡPëPNëPsPj PePsCḡC,PëPePsCḡC,PµCḡPsC—PrC-PI PSPµ CḡP»C-Pr PïCḡPëPiPëPSCµC,Pë,
PjPsP¶Pµ PSP°PIC-C,CHb P±CíC,Pë PïPsC,CḡC-P±PSPµ P·P±C-P»CHbCëPµPSPSCµ C—C...
PrPsP·Pë.

PḡC-Cḡ

Pj CḡP°P·C- PePsPSC,P°PeC,Cí P· C...PIPsCḡPëPj PSP° PeC-Cḡ PïP°C†C-C"psc,Pë P·
PïPsCḡCíCëPµPSPëPj C-PjCíPSC-C,PµC,PsPj PïPsPIPëPSPSC-, Cí CḡP°P·C-
PjPsP¶P»PëPiPsCḡC-, PsC,CḡPëPjP°C,Pë C-PS'C"PeC†C-Cḡ PSPsCḡPjP°P»CHbPSPsPiPs
C-PjCíPSPsPiP»PsP±CíP»C-PSCí CµPePsPjPsPiP° CḡP°PSC-CëPµ PïC-CḡP»Cµ
PePsPSC,P°PeC,Cí.

P'P°PeC†PëPSPë

PµP°C†C-C"psc,P°Pj, CµPeC- C,CḡPëPIP°P»PëPNë C‡P°Cḡ PïCḡPëPNëPjP°CḡC,CHb
PiP»CḡPePsPePsCḡC,PëPePsC—PrPë, PSPµ CḡP»C-Pr PIPiPsPrPëC,Pë P¶PëPIC- PIP°PeC†PëPSPë.
P'PëCḡPsP±P»PµPSPSCµ P°PSC,PëC,C-P» Cí PIC-PrPïPsPIC-PrCHb PSP° C-PSCëC-
PIP°PeC†PëPSPë PjPsP¶Pµ P±CíC,Pë P·PSPëP¶PµPSP°.

PµP°C†C-C"psc,Pë P· CḡPsP·P»P°PrP°PjPë C„CíPSPeC†C-C— PïPµC‡C-PSPePë

P'PëC...PsPrCµC‡Pë P· PrPsCḡPIC-PrCí, PsC,CḡPëPjP°PSPsPiPs Cí PïP°C†C-C"psc,C-PI P·
PiPµCḡPIPëPSPSPëPj P±C-P»C-P°CḡPSPëPj C†PëCḡPsP·PsPj (PµP'P!) PïC-P·PSCḡPsC—
CḡC,P°PrC-C—, P· C†PëCḡPsP·PsPj PïPµC‡C-PSPePë, CḡP»C-Pr PsC‡C-PeCíPIP°C,Pë
PïC-PrPIPëC%PµPSPsC— CḡPëCḡC,PµPjPSPsC— P±C-PsPrPsCḡC,CíPïPSPsCḡC-,
P±CíPrPµCḡPsPSC-PrCí Cí PICḡC-C... PïP°C†C-C"psc,C-PI P· CḡPµCḡPNëPsP·PSPs
PïPsCḡCíCëPµPSPsCḡ C„CíPSPeC†C-C"ḡ PïPµC‡C-PSPePë.

PhPrPSP°Pe Cí PïP°C†C-C"psc,C-PI P· C...PIPsCḡPsP±PsCḡ PïPµC‡C-PSPePë P±PµP·
C†PëCḡPsP·Cí P±CíPrPµCḡPsPSC-Pr Cí PrPµPSPSC-PNë PrPsP·C- 9 PjPi P±CíPI
P±PµP·PiPµC‡PSPëPNë C- PrPsP±CḡPµ PiPµCḡPµPSPsCḡPëPICḡCµ. PkPµPjP°C" PSC-CµPePëC...

PrP°PSPëC... PïCḡPs PSPµPsP±C...C-PrPSC-CíC,CH PsCíPsP±P»PëPIPëC...
CḡPµPePsPjPµPSPPrP°C†C-PNë C%PsPrPs PrPsP·CíPIP°PSPSCḡ PrP»Cḡ PïP°C†C-C"°PSC,C-PI P·
PSPµC†PëCḡPsC,PëC†PSPëPjPë P·P°C...PIPScḡCḡPIP°PSPSCḡPjPë PïPµC†C-PSPePë P°P±Ps P·
PSPµP·PSP°C†PSPëPjPë PïPsCḡCíCëPµPSPSCḡPjPë C,,CíPSPëC†C-C— PïPµC†C-PSPePë.

PµP°C†C-C"°PSC,Pë P· PïPsCḡCíCëPµPSPSCḡPj P·PsCḡCí

PµPsCḡCíCëPµPSPSCḡ P·PsCḡCí PjPsPḡP»PëPIC- PïCḡPë CíPëCíC,PµPjPSPsPjCí C,P°
PjC-CíC†PµPIPpsPjCí P·P°CíC,PsCíCíPIP°PSPSC- PePsCḡC,PëPePsCíC,PµCḡPsC—PrC-PI.
PïPeC%Ps Cí PïP°C†C-C"°PSC,P° CíPïPsCíC,PµCḡC-PiP°CḡC,CHCíCḡ C,P°PeC-
CíPëPjPïC,PsPjPë, CḡPe PïPsPjCíC,PSC-PSPSCḡ P·PsCḡCí P°P±Ps C-PSCëC-
PïPsCḡCíCëPµPSPSCḡ P·PsCḡCí, PIC-PS PïPsPIPëPSPµPS P·PIPµCḡPSCíC,PëCíCḡ PrPs
PsC,,C,P°P»CHPjPsP»PsPiP° PrP»Cḡ PsC†C-PSPePë PjPsPḡP»PëPIPëC... PïCḡPëC†PëPS, CḡPeC-
PjPsPḡCíC,CH PIPeP»CḡC†P°C,Pë PeP°C,P°CḡP°PeC,Cí, PiP»P°CíPePsPjCí P°P±Ps
CḡC-PrPeC-CíPSC- P·P°C...PIPScḡCḡPIP°PSPSCḡ, C,P°PeC- CḡPe C†PµPSC,CḡP°P»CHPSP°
CíPµCḡPsP·PSP° C...PsCḡC-PsCḡPµC,PëPSPsPïP°C,C-Cḡ (PïPḡP·P), PïCḡPs CḡPeC-
PïPsPIC-PrPsPjP»CḡP»PsCíCḡ PïC-CíP»Cḡ P·P°CíC,PsCíCíPIP°PSPSCḡ CíPëCíC,PµPjPSPëC...
C,P° PjC-CíC†PµPIPëC... PePsCḡC,PëPePsCíC,PµCḡPsC—PrC-PI.

P†PSCëC-

PµPsCḡC,PëPePsCíC,PµCḡPsC—PrPë PjPsPḡCíC,CH PïCḡPëP·PIPµCíC,Pë PrPs
PïCḡPëPiPSC-C†PµPSPSCḡ PsCíC- PiC-PïPsC,P°P»P°PjCíCí-PiC-PïPsC,,C-P·-
PSP°PrPSPëCḡPePsPIC- P·P°P»PsP·Pë C- PïCḡPëPiPSC-C†CíPIP°C,Pë CḡPµP°PeC†C-Cḡ PSP°
CíC,CḡPµCí. PµP°C†C-C"°PSC,P°Pj, CḡPeC- PiC-PrPrP°CḡC,CHCíCḡ
C...C-CḡCíCḡPiC-C†PSPsPjCí PIC,CḡCíC†P°PSPSCḡ P°P±Ps C-PSCëPëPj CíC,CḡPµCíP°Pj,
CḡPµPePsPjPµPSPPrCíC",CHCíCḡ PrPsPrP°C,PePsPIPµ CíPëCíC,PµPjPSPµ
P»C-PeCíPIP°PSPSCḡ PiP»CḡPePsPePsCḡC,PëPePsC—PrP°PjPë.

PḡP»C-Pr CíPSPëPeP°C,Pë CíCíPïCíC,PSCHPsPiPs P»C-PeCíPIP°PSPSCḡ
PePµC,PsPePsPSP°P·PsP»PsPj P°P±Ps C-PSCëPëPjPë C-PSPiC-P±C-C,PsCḡP°PjPë CYP3A4.

P'CíPrPµPSPsC,,P°P»CHPe 3 PjPi PjC-CíC,PëC,CH P»P°PeC,PsP·Cí C- CíP°C...P°CḡPsP·Cí.

PµCḡPµPïP°CḡP°C, PSPµ CíP»C-Pr PïCḡPëPNëPjP°C,Pë PïP°C†C-C"°PSC,P°Pj P·
CḡC-PrPeC-CíPSPëPjPë CíPïP°PrPePsPIPëPjPë CíC,P°PSP°PjPë
PSPµPïPµCḡPµPSPsCíPëPjPsCíC,C- PiP°P»P°PeC,PsP·Pë P°P±Ps C,,CḡCíPeC,PsP·Pë,
PSPµPrPsCíC,P°C,PSC-CíC,Cḡ CíP°C...P°CḡP°P·Pë-C-P·PsPjP°P»CHC,P°P·Pë P°P±Ps
PjP°P»CHP°P±CíPsCḡP±C†C-C"°Cḡ PiP»CḡPePsP·Pë-PiP°P»P°PeC,PsP·Pë, P° C,P°PePsPḡ C-P·
P·P°PiP°P»CHPSPsCḡ P»P°PeC,P°P·PSPsCḡ PSPµPrPsCíC,P°C,PSC-CíC,Cḡ.

PµP°C†C-C"°PSC,P°Pj P· P°CíC,PsC-PjCíPSPSPëPj PiPµPïP°C,PëC,PsPj CíP»C-Pr
CḡPµPiCíP»CḡCḡPSPs PePsPSC,CḡPsP»CḡPIP°C,Pë CḡC-PIPµPSCḡ C,CḡP°PSCíP°PjC-PSP°P·
(P°P»P°PSC-PSP°PjC-PSPsC,CḡP°PSCíC,,PµCḡP°P·Pë,
P°CíPïP°CḡC,P°C,P°PjC-PSPsC,CḡP°PSCíC,,PµCḡP°P·Pë (PḡP»Pḡ, PḡPḡPḡ) Cí
CíPëCḡPsPIP°C,C†C- (PePsPḡPSC-B B B B B B B 2 C,PëPḡPSC- PïCḡPsC,CḡPiPsPj
PïPµCḡCëPsPiPs PjC-CíCḡC†Cḡ P»C-PeCíPIP°PSPSCḡ C-, CḡPe PjC-PSC-PjCíPj, C†PµCḡPµP·
PePsPḡPSC- 3 PjC-CíCḡC†C- PI PïPsPrP°P»CHCëPsPjCí) P· PjPµC,PsCḡ PjPsPḡP»PëIPsC—
PePsCḡPµPeC†C-C— PrPsP·CíPIP°PSPSCḡ P±CíPrPµCíPsPSC-PrCí.

PµCḡPëPNëPsPj PïCḡPµPïP°CḡP°C,Cí P'CíPrPµPSPsC,,P°P»CHPe 3 PjPi PjPsPḡPµ
PïCḡPëP·PIPµCíC,Pë PrPs PïPsP·PëC,PëIPSPëC... CḡPµP·CíP»CHC,P°C,C-PI PrPsPïC-PSPi-

C,PμCΓC,C-PI.

*P—P°CΓC,PsCΓC¿PIP°PSPSCЦ C¿ PιPμCḡC-PsPr PIP°PiC-C,PSPSCΓC,C- P°P±Ps
PiPsPrC¿PIP°PSPSCЦ PiCḡC¿PrPrCḡ.*

P'P°PiC-C,PSC-CΓC,CH

P'CrPrPμPSPsC,,P°P»CHPe PSPμ PjPsP¶PSP° P·P°CΓC,PsCΓPsPICrPIP°C,Pē PιCḡPē
PIP°PiC-C,PSPSCΓC,C-, CЦPeC%Ps C,C-P»CHPePē C†Pμ PSPμ C" P°P±CΓPsP»CḡC,PSPs
PSPμPsP±C...C-PrPSPēPj. P"°PSC- PιCḡPs PIPiP»PēPI PιPμCḡPsCḡP°P»CHPSPsPiPs
PιCḡPēPμPsPjCr P±CrPrPμCΓPsPSC-PrCr PSP° PIP°PiC-C,PSC-CΓC,CH Cr P»CḡPrPēPSPē
PSPsCΓCЦC,CH PsP±PjPμP¶PμPSPēPμ C...P°CḡP°PeC,PμCḡ. P"°PSC- PιCḡPs
PIPēPePsCḡPēCΓC,P°PSPSCЦ C-PSPiP°P»CЦC†C-PμPSPsPiPs P±CrPrPμCΓPsPSC-PrCr
PIPμP»PēPePsCḡ PeC-P»CHPeC-CΓC,Cḡ PIP°PiC-C,PSPēC... P¶C-PSPsPe PIPeP°P·CrCḡC,CH
PSP° PIC-PrCΓCrC,PSC-CΓC,CH PSPμPiP°C,PēPIPSsPiPs PIPiP»PēPICr, PιCḡPsC,Pμ
PjP°PeCΓPēPjP°P»CHPSP° PePsPSC†PμPSC,CḡP°C†C-CЦ P±CrPrPμCΓPsPSC-PrCr PI
PιP»P°P·PjC-, CЦPe PsC†C-PeCrC"C,CHCΓCЦ, PιCḡPē PιCḡPēPμPsPjC-
P'CrPrPμPSPsC,,P°P»CHPeCr 3 PjPi P±CrPrPμ PIPēC%PsCḡ PI PιPsCḡC-PIPSCЦPSPSC- P·
C-PSPiP°P»CЦC†C-PμPSPēPj P±CrPrPμCΓPsPSC-PrPsPj. Pj C,PIP°CḡPēPS P±CrP»Ps
PιPsPeP°P·P°PSPs, C%Ps P±CrPrPμCΓPsPSC-Pr, CЦPe C- C-PSC€C-
PiP»CḡPePsPePsCḡC,PēPePsC—PrPē, PIPēPeP»PēPeP°C" P°PSPsPjP°P»C-C— CḡPsP·PIPēC,PeCr
PιP»PsPrP°. PιPePsCḡ PjC-CḡPsCḡ C,P°PeC- CЦPIPēC%P° PjPsP¶CrC,CH
CΓPiPsCΓC,PμCḡC-PiP°C,PēCΓCЦ Cr P»CḡPrPēPSPē, PICΓC,P°PSPsPIP»PμPSPs PSPμ P±CrP»Ps.
P-C-PSPeP°Pj CḡPμPιCḡPsPrCrPeC,PēPIPSsPiPs PIC-PeCr PιPμCḡPμPr PιPsC†P°C,PePsPj
P»C-PeCrPIP°PSPSCЦ P'CrPrPμPSPsC,,P°P»CHPePsPj CΓP»C-Pr PIPēPeP»CḡC†PēC,Pē
PjPsP¶P»PēPICr PIP°PiC-C,PSC-CΓC,CH C- PιCḡPsC,CЦPiPsPj P»C-PeCrPIP°PSPSCЦ
PSPμPsP±C...C-PrPSPs P·P°CΓC,PsCΓPsPICrPIP°C,Pē PIC-PrPιPsPIC-PrPSC-
PePsPSC,CḡP°C†PμPiC,PēPIPSC- P·P°CΓPsP±Pē.

P"PsPrC¿PIP°PSPSCЦ PiCḡC¿PrPrCḡ

P'CrPrPμCΓPsPSC-Pr PIPēPIPsPrPēC,CHCΓCЦ P· PsCḡPiP°PSC-P·PjCr P»CḡPrPēPSPē P·
PiCḡCrPrPSPēPj PjPsP»PsPePsPj (C-CΓPSCrCḡC,CH PrP°PSC- PιPs PμPeCΓPeCḡPμC†C-C—
C†CHPsPiPs PιCḡPμPiP°CḡP°C,Cr PιC-CΓP»CЦ C-PSPiP°P»CЦC†C-PμPSPsPiPs
P·P°CΓC,PsCΓCrPIP°PSPSCЦ). PμCḡPsC,Pμ P·PSP°C†PSPsPiPs PIPiP»PēPICr PιC-CΓP»CЦ
PιCḡPēPμPsPjCr P'CrPrPμPSPsC,,P°P»CHPeCr 3 PjPi Cr PjPμP¶P°C...
C,PμCḡP°PιPμPIC,PēC†PSPsPiPs PrC-P°PιP°P·PsPSCr PSP° PrPēC,PēPSCr, CЦPeCr
PiPsPrCrCḡC,CH C,P°PePēPj PjPsP»PsPePsPj, PSPμ PsC†C-PeCrC"C,CHCΓCЦ. P C-C€PμPSPSCЦ
PιCḡPs C,Pμ, C†Pē CΓP»C-Pr PιCḡPēPιPēPSPēC,Pē PiCḡCrPrPSPμ PIPēPiPsPrPsPICrPIP°PSPSCЦ
P°P±Ps C†Pē PιPμCḡPμCḡPIP°C,Pē PιCḡPēPμPsPj P'CrPrPμCΓPsPSC-PrCr P°P±Ps
CrC,CḡPēPjP°C,PēCΓCЦ PIC-Pr C,PμCḡP°PiC-C—, CΓP»C-Pr PιCḡPēPμPjP°C,Pē P·
CrCḡP°C...CrPIP°PSPSCЦj PePsCḡPēCΓC,C- PiCḡCrPrPSPsPiPs PIPēPiPsPrPsPICrPIP°PSPSCЦ
PrP»CЦ PrPēC,PēPSPē C- PePsCḡPēCΓC,C- C,PμCḡP°PiC-C— PrP»CЦ P¶C-PSPePē.

PαPμCḡC,PēP»CHPSC-CΓC,CH

PκPμPjP°C" PrP°PSPēC... PιCḡPs PIPiP»PēPI P±CrPrPμCΓPsPSC-PrCr PSP°
C,,PμCḡC,PēP»CHPSC-CΓC,CH P»CḡPrPēPSPē. P>C-PeCrPIP°PSPSCЦ P±CrPrPμCΓPsPSC-PrPsPj
PSPμ PIPiP»PēPIP°P»Ps PSP° C,,PμCḡC,PēP»CHPSC-CΓC,CH Cr PrPsCΓP»C-PrP¶PμPSPSCЦC...
PSP° C,PIP°CḡPēPSP°C....

$P - Pr^{\circ}C, PSC - Cl^{\circ}C, CH \text{ PIPiP} \gg P \ddot{e}PIP^{\circ}C, P \ddot{e} PSP^{\circ} C \epsilon PIP \ddot{e} PrPeC - Cl^{\circ}C, CH \text{ C} \ddot{H} P \mu P^{\circ} PeC \dagger C - C - P \ddot{i}C \ddot{H} P \ddot{e}$
 $PeP \mu C \ddot{H} C \acute{z} PIP^{\circ} PSPSC - P^{\circ} PIC, PsC, C \ddot{H} P^{\circ} PSC \acute{I} P \ddot{i} PsC \ddot{H} C, PsPj P^{\circ} P \pm Ps C - PSC \epsilon P \ddot{e} PjP \ddot{e}$
 $PjP \mu C \dots P^{\circ} PSC - P \cdot PjP^{\circ} PjP \ddot{e}.$

$P \acute{k} P \mu P \ddot{i} C \ddot{H} PsPIP sPrP \ddot{e} P \gg PsCl^{\circ} Cl \ddot{i} P \P PsPrPSP \ddot{e} C \dots PrPsCl^{\circ} P \gg C - PrP \P P \mu PSC \ddot{H} PIPiP \gg P \ddot{e} PIC \acute{I} PSP^{\circ}$
 $P \cdot PrP^{\circ} C, PSC - Cl^{\circ}C, CH \text{ PeP} \mu C \ddot{H} C \acute{I} PIP^{\circ} C, P \ddot{e} P^{\circ} PIC, PsC, C \ddot{H} P^{\circ} PSC \acute{I} P \ddot{i} PsC \ddot{H} C, PsPj C, P^{\circ}$
 $PIP \ddot{e} PePsC \ddot{H} P \ddot{e} Cl^{\circ}C, PsPIC \acute{I} PIP^{\circ} C, P \ddot{e} C - PSC \epsilon C - PjP \mu C \dots P^{\circ} PSC - P \cdot PjP \ddot{e}. P \ddot{h} P \gg P \mu PsCl^{\circ} PeC - P \gg CHPeP \ddot{e}$
 $PjPsP \P P \gg P \ddot{e} PIP \mu PIP \ddot{e} PSP \ddot{e} PePSP \mu PSPSC \ddot{i} PrP \mu Cl \ddot{i} PeP \ddot{e} C \dots P \ddot{i} PsP \pm C - C \ddagger PSP \ddot{e} C \dots P \mu C, P \mu PeC, C - PI,$
 $P \ddot{i} PsC, C \ddot{H} C - P \pm PSPs P \pm C \acute{I} C, P \ddot{e} C \acute{I} PIP^{\circ} P \P PSP \ddot{e} Pj C, P^{\circ} PsC \dagger C - PSC \ddot{H} PIP^{\circ} C, P \ddot{e} Cl^{\circ} PIC - P \ddot{N} \ddot{e} Cl^{\circ}C, P^{\circ} PS$
 $P \ddot{i} P \mu C \ddot{H} P \mu Pr C, P \ddot{e} Pj, Cl \ddot{i} Pe PeP \mu C \ddot{H} C \acute{I} PIP^{\circ} C, P \ddot{e} C, C \ddot{H} P^{\circ} PSC \acute{I} P \ddot{i} PsC \ddot{H} C, PSP \ddot{e} Pj P \cdot P^{\circ} Cl^{\circ} PsP \pm PsPj$
 $P^{\circ} P \pm Ps P \ddot{i} C \ddot{H} P^{\circ} C \dagger CHIP^{\circ} C, P \ddot{e} P \cdot C - PSC \epsilon P \ddot{e} PjP \ddot{e} PjP \mu C \dots P^{\circ} PSC - P \cdot PjP^{\circ} PjP \ddot{e}.$

$P \ddot{Y} P \ddot{i} PsCl^{\circ} C - P \pm P \cdot P^{\circ} Cl^{\circ} C, PsCl^{\circ} C \acute{z} PIP^{\circ} PSPSC \ddot{i} C, P^{\circ} PrPsP \cdot P \ddot{e}.$

$P \Gamma PIPsC \ddot{H} PsP \pm P^{\circ} P \ddot{h} C \ddot{H} PsPSP^{\circ}$

$P \dagger PSPrC \acute{z} PeC \dagger C - Cl \ddot{i} C \ddot{H} P \mu PjC - Cl^{\circ}C - C -$

$P P \mu PePsPjP \mu PSPrPsPIP^{\circ} PSP^{\circ} PrPsP \pm PsPIP^{\circ} PrPsP \cdot P^{\circ} Cl^{\circ} C, P^{\circ} PSPsPIP \ddot{e} C, CH \text{ P} \ddot{i} Ps 3$
 $PeP^{\circ} P \ddot{i} Cl^{\circ} C \acute{I} P \gg P \ddot{e} 1 C \ddot{H} P^{\circ} P \cdot PSP^{\circ} PrP \mu PSC \ddot{H} PIC \ddot{H} P^{\circ} PSC \dagger C - P^{\circ} P \pm Ps P \ddot{i} Ps 1 PeP^{\circ} P \ddot{i} Cl^{\circ} C \acute{I} P \gg C - (C \% Ps$
 $PjC - Cl^{\circ}C, Cl \ddot{i} C, CH 3 PjPi P \pm C \acute{I} PrP \mu Cl^{\circ} PsPSC - PrC \acute{I}) 3 C \ddot{H} P^{\circ} P \cdot P \ddot{e} PSP^{\circ} PrP \mu PSC \ddot{H}$
 $(P \mu PePIC - PIP^{\circ} P \gg P \mu PSC, PSPs P \cdot P^{\circ} P \ddot{i} P^{\circ} P \gg CHPSC - P \ddot{N} \ddot{e} PrP \mu PSPSC - P \ddot{N} \ddot{e} PrPsP \cdot C - 9 PjPi$
 $P \pm C \acute{I} PrP \mu Cl^{\circ} PsPSC - PrC \acute{I}) (PIC \ddot{H} P^{\circ} PSC \dagger C -, PIPrP \mu PSC \ddot{H} C - C \acute{I} PIP \mu C \ddagger P \mu C \ddot{H} C -), Cl \ddot{i} PeC \% Ps C \dagger P \mu$
 $P \pm C - P \gg CHC \epsilon P \cdot C \ddot{H} C \acute{I} C \ddagger PSPs PrP \gg Cl \ddot{i} P \ddot{i} P^{\circ} C \dagger C - C''PSC, P^{\circ}.$

$P \ddot{y} C \ddot{H} P \ddot{e} PIP^{\circ} P \gg C - Cl^{\circ}C, CH \text{ P} \cdot P^{\circ} Cl^{\circ} C, PsCl^{\circ} C \acute{z} PIP^{\circ} PSPSC \ddot{i}$

$P \ddot{y} C \ddot{H} P \ddot{e} PIP^{\circ} P \gg C - Cl^{\circ}C, CH \text{ P} \gg C - PeC \acute{I} PIP^{\circ} PSPSC \ddot{i} P \cdot P^{\circ} P \cdot PIP \ddot{e} C \ddagger P^{\circ} P \ddot{N} \ddot{e} Cl^{\circ}C, P^{\circ} PSPsPIP \ddot{e} C, CH 8$
 $C, P \ddot{e} P \P PSC - PI.$

$P \ddot{h} C - PeC \ddot{H} PsCl^{\circ} PePsP \ddot{i} C - C \ddagger PSP \ddot{e} P \ddot{N} \ddot{e} PePsP \gg C - C,$

$P \dagger PSPrC \acute{z} PeC \dagger C - Cl \ddot{i} C \ddot{H} P \mu PjC - Cl^{\circ}C - C -$

$P P \mu PePsPjP \mu PSPrPsPIP^{\circ} PSP^{\circ} PrPsP \pm PsPIP^{\circ} PrPsP \cdot P^{\circ} Cl^{\circ} C, P^{\circ} PSPsPIP \ddot{e} C, CH 3 PeP^{\circ} P \ddot{i} Cl^{\circ} C \acute{I} P \gg P \ddot{e} 1$
 $C \ddot{H} P^{\circ} P \cdot PSP^{\circ} PrP \mu PSC \ddot{H} PIC \ddot{H} P^{\circ} PSC \dagger C - P \ddot{i} P \mu C \ddot{H} P \mu Pr Cl^{\circ} PSC - PrP^{\circ} PSPePsPj (PIC - PrP \ddot{i} PsPIC - PrP^{\circ} C''$
 $PrPsP \pm PsPIC - P \ddot{N} \ddot{e} PrPsP \cdot C - 9 PjPi P \pm C \acute{I} PrP \mu Cl^{\circ} PsPSC - PrC \acute{I}).$

$P \mu C - PrC, C \ddot{H} P \ddot{e} PjP^{\circ} PSPSC \ddot{i} C \ddot{H} P \mu PjC - Cl^{\circ}C - C -$

$P \mu C - PrC, C \ddot{H} P \ddot{e} PjC \acute{I} C \ddot{H} C \ddagger C \acute{I} C, P \mu C \ddot{H} P^{\circ} P \ddot{i} C - C \ddot{H} Cl^{\circ} P \gg C - Pr C \ddot{H} PsP \cdot P \ddot{i} PsC \ddagger P \ddot{e} PSP^{\circ} C, P \ddot{e} P \gg P \ddot{e} C \epsilon P \mu C \acute{I}$
 $P \ddot{i} P^{\circ} C \dagger C - C''PSC, C - PI P \cdot C \ddagger P^{\circ} Cl^{\circ} C, Ps C \ddot{H} P \mu C \dagger P \ddot{e} PrP \ddot{e} PIC \acute{I} C \ddot{H} C \ddagger P \ddot{e} PjP \ddot{e} Cl^{\circ} P \ddot{e} PjP \ddot{i} C, PsPjP^{\circ} PjP \ddot{e}$
 $PjC - PeC \ddot{H} PsCl^{\circ} PePsP \ddot{i} C - C \ddagger PSPsPiPs PePsP \gg C - C, C \acute{I} P \ddot{i} C - Cl^{\circ} P \gg C \ddot{i} C \acute{I} P \ddot{i} C - C \epsilon PSPsPiPs$
 $C - PSPrC \acute{I} PeC \dagger C - P \ddot{N} \ddot{e} PSPsPiPs P \gg C - PeC \acute{I} PIP^{\circ} PSPSC \ddot{i}. P - P^{\circ} P \gg P \mu P \P PSPs PIC - Pr$
 $C - PSPrP \ddot{e} PIC - PrC \acute{I} P^{\circ} P \gg CHPSP \ddot{e} C \dots P \ddot{i} PsC, C \ddot{H} P \mu P \pm P \ddot{i} P^{\circ} C \dagger C - C''PSC, P^{\circ} PjPsP \P PSP^{\circ}$
 $P \cdot P^{\circ} Cl^{\circ} C, PsCl^{\circ} PsPIC \acute{I} PIP^{\circ} C, P \ddot{e} Cl^{\circ} C \dots P \mu PjC \acute{I} PrPsP \cdot C \acute{I} PIP^{\circ} PSPSC \ddot{i}: PrPIC - PeP^{\circ} P \ddot{i} Cl^{\circ} C \acute{I} P \gg P \ddot{e}$
 $PsPrP \ddot{e} PS C \ddot{H} P^{\circ} P \cdot PSP^{\circ} PrPsP \pm C \acute{I} PIC \ddot{H} P^{\circ} PSC \dagger C - (6 PjPi P \pm C \acute{I} PrP \mu Cl^{\circ} PsPSC - PrC \acute{I}) P^{\circ} P \pm Ps PrPIC -$
 $PeP^{\circ} P \ddot{i} Cl^{\circ} C \acute{I} P \gg P \ddot{e} PsPrP \ddot{e} PS C \ddot{H} P^{\circ} P \cdot PSP^{\circ} PrPsP \pm C \acute{I} PIC \ddot{H} P^{\circ} PSC \dagger C -, C \ddagger P \mu C \ddot{H} P \ddot{i} C \acute{I} C \ddot{H} C \ddagger P \ddot{e} P \cdot$
 $PsPrPSC - C''C \ddot{H} PeP^{\circ} P \ddot{i} Cl^{\circ} C \acute{I} P \gg PsC \ddot{H} PSP^{\circ} PrPsP \pm C \acute{I} PIC \ddot{H} P^{\circ} PSC \dagger C - (C \% Ps PIC - PrP \ddot{i} PsPIC - PrP^{\circ} C''$

$P''P \gg C \parallel C - P \text{SP} \text{Pr} \text{Cr} \text{Pe} \text{C} \uparrow \text{C} - C - \text{C} \text{H} \text{P} \mu \text{Pj} \text{C} - \text{C} \uparrow \text{C} - C - \text{C} \uparrow \text{P} \gg \text{C} - \text{Pr} \text{Pi} \text{C} \text{H} \text{P} \text{P} \text{P} \cdot \text{PSP}^\circ \text{C} \uparrow \text{P}^\circ \text{C}, \text{P} \text{P} \cdot \text{P}^\circ \text{Pi} \text{P}^\circ \text{P} \gg \text{C} \text{H} \text{P} \text{SCr} \text{Pr} \text{Ps} \text{P} \pm \text{Ps} \text{PICr} \text{Pr} \text{Ps} \text{P} \cdot \text{Cr} \text{ } 9 \text{Pj} \text{Pi} \text{Pr} \text{Ps} \text{Pr} \text{Ps} \text{C} \uparrow \text{C} \parallel \text{Pi} \text{PSP} \mu \text{PSPSC} \parallel$
 $\text{C} \text{H} \text{P} \mu \text{Pj} \text{C} - \text{C} \uparrow \text{C} - C - \text{P} \mu \text{C} - \text{C} \uparrow \text{P} \gg \text{C} \parallel \text{C} \uparrow \text{C} \text{H} \text{Ps} \text{Pi} \text{Ps} \text{Pr} \text{P} \gg \text{C} \parallel \text{Pi} \text{C} - \text{Pr} \text{C}, \text{C} \text{H} \text{P} \text{P} \text{Pj} \text{P}^\circ \text{PSPSC} \parallel$
 $\text{C} \text{H} \text{P} \mu \text{Pj} \text{C} - \text{C} \uparrow \text{C} - C - \text{C} \uparrow \text{P} \gg \text{C} - \text{Pr} \text{Pi} \text{C} \text{H} \text{P} \text{P} \text{P} \cdot \text{PSP}^\circ \text{C} \uparrow \text{P}^\circ \text{C}, \text{P} \text{P} \cdot \text{P}^\circ \text{Pi} \text{P}^\circ \text{P} \gg \text{C} \text{H} \text{P} \text{SCr} \text{Pr} \text{Ps} \text{P} \pm \text{Ps} \text{PICr} \text{Pr} \text{Ps} \text{P} \cdot \text{Cr} \text{ } 6 \text{Pj} \text{Pi} \text{P} \pm \text{Cr} \text{Pr} \text{P} \mu \text{C} \uparrow \text{Ps} \text{PSC} - \text{Pr} \text{Cr} \text{P} \cdot \text{C} - \text{Pe} \text{Cr} \text{PIP}^\circ \text{PSPSC} \parallel \text{Pr} \text{P} \gg \text{C} \parallel \text{Pi} \text{C} - \text{Pr} \text{C}, \text{C} \text{H} \text{P} \text{P} \text{Pj} \text{P}^\circ \text{PSPSC} \parallel$
 $\text{C} \text{H} \text{P} \mu \text{Pj} \text{C} - \text{C} \uparrow \text{C} - C - \text{Pi} \text{C} \text{H} \text{P} \text{P} \text{P}^\circ \text{Cr} \text{C}, \text{Ps} \text{C} - \text{Pj} \text{Cr} \text{PSPSPs} \text{Pj} \text{Cr} \text{Pi} \text{P} \mu \text{Pi} \text{P}^\circ \text{C}, \text{P} \text{P} \text{C}, \text{C} - \text{C} \uparrow \text{P} \gg \text{C} - \text{Pr}$

ΠῖCῆPsPrPsPIP¶CῖP°P,Πῆ C%PsPSP°PNῆPjPμPSCεPμ ΠῖCῆPsC,CῖPῖPsPj 24 PjC-CῖCῖCῖCῖC-PI.
P™PsPiPs PjPsP¶PSP° ΠῖCῆPῆPῖPῆPSPῆC,Πῆ P»ΠῆCεPμ P·P° CῖPjPsPIPῆ ΠῖPsCῖC,C-PNῆPSPsC—
P±C-PsC...C-PjC-C‡PSPsC— CῆPμPjC-CῖC-C— C,P° PIC-PrCῖCῖC,PSPsCῖC,C- PsP·PSP°Pε
P·P°PῖP°P»PμPSPSCῖ Πῖ P±C-PsΠῖCῖC-C— ΠῖPμC‡C-PSPePῆ.

PμCῆPῆPῖPῆPSPμPSPSCῖ P»C-PεCῖPIP°PSPSCῖ

P>C-PεCῖPIP°PSPSCῖ ΠῖCῆPμPῖP°CῆP°P,PsPj P'CῖPrPμPSPsC,,P°P»CHPe 3 PjPi PSPμ CῖP»C-Pr
ΠῖCῆPῆPῖPῆPSCῖC,Πῆ CῆC-P·PePs, P° PIC-PrPjC-PSCῖC,Πῆ ΠῖPsCῖC,CῖPῖPsPIPs
(P·PSPῆP¶PμPSPSCῖPj PrPsP·Pῆ). P PμPePsPjPμPSPrCῖC"C,CHCῖCῖ ΠῖPsCῖC,CῖPῖPsPIPμ
P·PSPῆP¶PμPSPSCῖ PrPsP·Pῆ ΠῖCῆPsC,CῖPῖPsPj 2 C,PῆP¶PSC-PI.

PμP°CῖC-C"PSC,Πῆ P· ΠῖPsCῆCῖCεPμPSPSCῖPj C,,CῖPSPεCῖC-C— PSPῆCῆPsPe

PῖPῖPμCῖPῆC,,C-C‡PSC- CῆPμPePsPjPμPSPrP°CῖC-C— C%PsPrPs PrPsP·CῖPIP°PSPSCῖ PrP»Cῖ
ΠῖP°CῖC-C"PSC,C-PI P· PSPῆCῆPePsPIPsCῆ PSPμPrPsCῖC,P°P,PSC-CῖC,Cῆ PIC-PrCῖCῖC,PSC-.

PμP°CῖC-C"PSC,Πῆ P· ΠῖPsCῆCῖCεPμPSPSCῖPj C,,CῖPSPεCῖC-C— ΠῖPμC‡C-PSPePῆ

PῖP»C-Pr PrPsC,CῆPῆPjCῖPIP°P,ΠῆCῖCῖC PsP±PμCῆPμP¶PSPsCῖC,C- C%PsPrPs
ΠῖP°CῖC-C"PSC,C-PI P· ΠῖPsCῆCῖCεPμPSPSCῖPj C,,CῖPSPεCῖC-C— ΠῖPμC‡C-PSPePῆ
P»PμΠῖPePsPiPs C,P° ΠῖPsPjC-CῆPSPsPiPs CῖC,CῖPῖPμPSCῖ.

-

PῖPῖPsCῖC-P± P·P°CῖC,PsCῖCῖPIP°PSPSCῖ

PμP°ΠῖCῖCῖP»Πῆ CῖP»C-Pr ΠῖCῆPῆPNῆPjP°P,Πῆ ΠῖCῆPῆP±P»ΠῆP·PSPs P·P° ΠῖC-PI ΠῖPsPrPῆPSPῆ
PrPs C—PrPῆ, PePsPIC,P°CῆC‡Pῆ C—C... CῖC-P»ΠῆPjPῆ C,P° P·P°PῖPῆPIP°CῆC‡Pῆ
PrPsCῖC,P°P,PSCHPsCῆ PeC-P»CHPeC-CῖC,Cῆ CῆC-PrPῆPSPῆ (PSP°ΠῖCῆPῆPeP»P°Pr
CῖPeP»CῖPSPεPsCῆ PIPsPrPῆ).

PμP°CῖC-C"PSC,Πῆ, CῖPeC- PjP°CῆC,CH C,CῆCῖPrPSPsC%C- P· PePsPIC,P°PSPSCῖPj
PeP°ΠῖCῖCῖP», PjPsP¶CῖC,CH PIC-PrPeCῆPῆC,Πῆ C—C... C- ΠῖCῆPῆPNῆPSCῖC,Πῆ P»ΠῆCεPμ
PePῆCεPePsPIPsCῆPsP·C‡PῆPSPSC- ΠῖCῆP°PSCῖP»Πῆ P· PrPsCῖC,P°P,PSCHPsCῆ
PeC-P»CHPeC-CῖC,Cῆ CῆC-PrPῆPSPῆ. PῖPμ PSPμ PIPῖP»ΠῆPIP°P,ΠῆPjPμ PSP°
PμC,,PμPeC,ΠῆPIPSC-CῖC,CH P'CῖPrPμPSPsC,,P°P»CHPeCῖ 3 PjPi.

P"C-C,Pῆ.

P'CῖPrPμPSPsC,,P°P»CHPe PSPμ CῖP»C-Pr P·P°CῖC,PsCῖPsPICῖPIP°P,Πῆ PrC-C,CῖPj PIC-PePsPj
PrPs 12 CῆPsPeC-PI C‡PμCῆPμP· PSPμPrPsCῖC,P°P,PSC-PNῆ PrPsCῖPIC-Pr C,P°
PNῆPjPsPIC-CῆPSPμ ΠῖC-PrPIPῆC%PμPSPSCῖ CῆPῆP·PῆPeCῖ ΠῖCῆPῆPῖPSC-C‡PμPSPSCῖ
PSP°PrPSPῆCῆPePsPIPῆC... P·P°P»PsP· Cῖ ΠῖP°CῖC-C"PSC,C-PI CῖC-C"C— PIC-PePsPIPsC—
ΠῖCῆCῖPῖPῆ.

P"C-C,Πῆ PIC-Pr 12 PrPs 18 CῆPsPeC-PI

P'PμP·ΠῖPμPeP° C,P° PμC,,PμPeC,ΠῆPIPSC-CῖC,CH P·P°CῖC,PsCῖCῖPIP°PSPSCῖ

$P'CrPrP_{\mu}PSPsC_{\mu}, P^{\circ}P \gg CHPeCr \ 3 \ PjPi \ PrC-C, CIPj \ PIC-PePsPj \ PIC-Pr \ 12 \ PrPs \ 18 \ C_{\eta}PsPeC-PI \ PSP_{\mu}$
 $PIC\acute{C}, P^{\circ}PSPsPIP \gg P_{\mu}PSP^{\circ}. P''PsC\acute{C}, CrP\ddot{I}PSC- \ PSP^{\circ} \ C\acute{C}HPSiPsPrPSC- \ PrP^{\circ}PSC- \ C\%_{\circ}PsPrPs$
 $P\ddot{I}C-PrP \gg C-C, PeC-PI \ (PIC-Pe \ 12-18 \ C_{\eta}PsPeC-PI) \ P \cdot \ C \dots PIPsC_{\eta}PsP \pm PsC_{\eta} \ P_{\eta}C_{\eta}PsPSP^{\circ} \ P^{\circ}P \pm Ps$
 $PiP_{\mu}P\ddot{I}P^{\circ}C, P\ddot{e}C, PsPj \ PSP^{\circ}PIP_{\mu}PrP_{\mu}PSC- \ PI \ C_{\eta}PsP \cdot PrC-P \gg P^{\circ}C \dots B \ll P_{\mu}PsP \pm C-C \ddagger PSC-$
 $C_{\eta}P_{\mu}P^{\circ}PeC\acute{C}-C-B \gg C- \ B \ll P \propto P^{\circ}C_{\eta}PjP^{\circ}PePsPrP\ddot{e}PSP^{\circ}PjC-PeP^{\circ}B \gg. \ P_{\eta}PrPSP^{\circ}Pe$
 $C_{\eta}P_{\mu}PePsPjP_{\mu}PSPPrP^{\circ}C\acute{C}-C- \ P \cdot \ PrPsP \cdot CrPIP^{\circ}PSPSC_{\eta} \ PIC-PrC\acute{C}C\acute{C}, PSC-.$

$P_{\mu}P_{\mu}C_{\eta}P_{\mu}PrPsP \cdot C \acute{C}PIP^{\circ}PSPSC_{\eta}.$

$P''PsC, P_{\mu}P\ddot{I}P_{\mu}C_{\eta} \ PSP_{\mu} \ P\ddot{I}PsPIC-PrPsPjP \gg CIP \gg PsC\acute{C}C_{\eta} \ P\ddot{I}C_{\eta}Ps \ PIP\ddot{e}P\ddot{I}P^{\circ}PrPeP\ddot{e}$
 $P\ddot{I}P_{\mu}C_{\eta}P_{\mu}PrPsP \cdot CrPIP^{\circ}PSPSC_{\eta} \ P'CrPrP_{\mu}PSPsC_{\mu}, P^{\circ}P \gg CHPePsPj. \ P- \ PsPiP \gg CIPPrC\acute{C} \ PSP^{\circ}$
 $PIP \gg P^{\circ}C\acute{C}, P\ddot{e}PIP sC\acute{C}, C- \ P'CrPrP_{\mu}PSPsC_{\mu}, P^{\circ}P \gg CHPeCr \ 3 \ PjPi \ P\ddot{I}P_{\mu}C_{\eta}P_{\mu}PrPsP \cdot CrPIP^{\circ}PSPSC_{\eta},$
 $CIPeP_{\mu} \ PjPsP_{\eta}P_{\mu} \ P\ddot{I}C_{\eta}P\ddot{e}P \cdot PIPsPrP\ddot{e}C, P\ddot{e} \ PrPs \ C, PsPeC\acute{C}P\ddot{e}C \ddagger PSPsPiPs \ C\acute{C}C_{\eta}P^{\circ}P_{\eta}P_{\mu}PSPSC_{\eta},$
 $PjP^{\circ}P \gg PsP_{\eta}PjPsPIC-C_{\eta}PSP_{\mu}.$

$P_{\mu}PsP \pm C-C \ddagger PSC- \ C_{\eta}P_{\mu}P^{\circ}PeC\acute{C}-C-.$

$P\ddot{S}P^{\circ}C\acute{C}, PsC, Cr \ P\ddot{I}PsP \pm C-C \ddagger PSP\ddot{e}C \dots C_{\eta}P_{\mu}P^{\circ}PeC\acute{C}-P_{\eta} \ PsC\acute{C}-PSC_{\eta}PIP^{\circ}P \gg P\ddot{e} \ C, P^{\circ}PeP\ddot{e}Pj$
 $C \ddagger P\ddot{e}PSPsPj:$

$PrC\acute{C}P_{\eta}P_{\mu} \ C \ddagger P^{\circ}C\acute{C}, Ps: \geq 1/10;$

$C \ddagger P^{\circ}C\acute{C}, Ps: \geq 1/100, < 1/10;$

$PSP_{\mu}C \ddagger P^{\circ}C\acute{C}, Ps: \geq 1/1000, < 1/100;$

$C_{\eta}C-PrPePs: \geq 1/10000, < 1/1000;$

$PrC\acute{C}P_{\eta}P_{\mu} \ C_{\eta}C-PrPePs: < 1/10000, PIPeP \gg C_{\eta}C \ddagger P^{\circ}C_{\eta}C \ddagger P\ddot{e} \ PsPeC_{\eta}P_{\mu}PjC-$
 $P\ddot{I}PsPIC-PrPsPjP \gg P_{\mu}PSPSC_{\eta}.$

$P_{\eta}P \gg P^{\circ}C\acute{C} \ C\acute{C}P\ddot{e}C\acute{C}, P_{\mu}PjP\ddot{e}$
 $PsC_{\eta}PiP^{\circ}PSC-PI$

$P\ddot{S}P^{\circ}C\acute{C}, PsC, P^{\circ}$
 $PIC-PrP\ddot{I}PsPIC-PrPSPs$
 $PrPs \ MedDRA$

$P_{\mu}PsP \pm C-C \ddagger PSC- \ C_{\eta}P_{\mu}P^{\circ}PeC\acute{C}-C-$

**РљР»Р°СЃ СЃРёСЃСЃ, РµРјРјРё
РѕСЃРјРёРѕРѕСЃ-Рј**

[illegible]

PSP^oClC,PsC,P^o
PIC-PrPiPsPIC-PrPSPs
PrPs MedDRA
PSP^oClC.Ps

$$P''CfP \parallel Pu \text{ CHC-PrPePs}$$
$$\text{P}_{\text{U}}\text{P}_{\text{S}}\text{C}_{\text{H}}\text{C}_{\text{r}}\text{C}_{\text{e}}\text{P}_{\text{u}}\text{P}_{\text{S}}\text{P}_{\text{S}}\text{C}_{\text{U}} \quad \text{P} \cdot \text{P}_{\text{S}}\text{C}_{\text{H}}\text{C}_{\text{r}}$$

P C-PΓPεPs

PĖP»CrPSPePsPIPs-PePëC€PePsPIC-
PïPsCĤCrC€PuPSPSCĤ

P§P°CΓC,P_s

$$P_k P_\mu C \pm P^\circ C \Gamma C, P_s$$
$$\begin{array}{c} \text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7 \\ \text{C}-\text{P}_{11}\text{C}_7\text{P}_{12}\text{P}_{13}\text{P}_{14}\text{C}_7-\text{C}_7\text{P}_{11}\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7 \\ \text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{P}_{14}\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7 \\ \text{C}_7\text{P}_{11}\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{P}_{14}\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{P}_{14}\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7 \\ \text{C}_7\text{P}_{11}\text{C}_7\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7\text{P}_{11}\text{P}_{12}\text{P}_{13}\text{C}_7\text{C}_7\text{C}_7 \end{array}$$

P C-PrPePs
P''CrP¶Pµ C7C-PrPePs
P§P°CΓC.Ps

PSP^oCΓC.Ps

$$\begin{array}{l} \text{P}_{\text{u}}\text{P}_{\text{s}}\text{C}\tilde{\text{h}}\text{C}\tilde{\text{r}}\text{C}\tilde{\text{e}}\text{P}_{\text{u}}\text{PSPSC}\tilde{\text{u}} \\ \text{PSP}_{\text{u}}\text{C}\tilde{\text{h}}\text{PIP}_{\text{s}}\text{PIP}_{\text{s}}\text{C} - \text{C}\tilde{\text{r}}\text{P}\tilde{\text{e}}\text{C}\tilde{\text{r}}\text{C}, \text{P}_{\text{u}}\text{P}_{\text{j}}\text{P}\tilde{\text{e}} \end{array}$$

P C-PrPePs
P§P°CÍC,P§
P''CfP¶Pµ CÍC-PrPePs

$$\begin{array}{l} \text{P}\ddot{\text{U}}\text{C}\dot{\text{I}}\text{P}\ddot{\text{e}}\text{C}\dots\text{C}-\text{C}\ddagger\text{PSC-} \\ \text{P}\ddot{\text{i}}\text{P}\text{sC}\dot{\text{H}}\text{C}\dot{\text{r}}\text{C}\text{€P}\text{uPSPSC}\text{H} \end{array}$$

PSP^oCΓC.Ps

$$P_k P_\mu C \pm P^\circ C \Gamma C, P_s$$
$$\begin{aligned} & \text{P}_{\mu}\text{PsC}\tilde{\eta}\text{CrC}\epsilon\text{P}_{\mu}\text{PSPSC}\Pi\text{ P}\cdot\text{P}\pm\text{PsPeCr} \\ & \text{C}\epsilon\text{PeC}-\text{C}\tilde{\eta}\text{P}\epsilon\text{ C-} \\ & \text{P}\dot{\text{C}}-\text{PrC}\epsilon\text{PeC}-\text{C}\tilde{\eta}\text{PSP}\epsilon\text{C... C.PeP}^{\circ}\text{PSP}\epsilon\text{PS} \end{aligned}$$

P C-PrP^{Sc}
P^{Sc}PrP^{Sc}, P^{Sc}

PŸCřPrPëPSPSC- PïPsCĤCřC€PuPSPSCLlP"ĆřP¶Pu CĤC-PrPePs

P C-PrPEPs

$$\begin{array}{c} \text{P} - \text{P}^{\circ} \text{PiP}^{\circ} \text{P} \gg \text{CHbPSC} - \\ \text{PiPsC} \text{ThCr} \text{C} \text{€PuPSPSC} \text{U} \end{array}$$
$$P''CrP\parallel P_{\mu}CHC-PrPePs$$
$$\mathbf{P_{II}P_{S}P_{\pm}C-C_{\mp}P_{S}C-CHP_{\mu}P^{\circ}P_{\epsilon}C_{\dagger}C-C-}$$

PŸPëPSPrCĤPsPj PᵼCfCēPēPSPiP°,
PjC-Cl̇Cl̇C†PμPiPsPrC-P±PSPμ
PsP±P»PēC‡C†C‡, PsP¶PēCĤC-PSPSC‡,
P·PSPēP¶PμPSPSC‡
PiP»CĤPePsP·PsC,PsP»PμCĤP°PSC,PSPsCl̇C,C-,
C†CfPeCĤPsPiPēPNē PrC-P°P±PμC,,
PiC-PrPiPēC%oPμPSPēPNē C,PēCl̇Pe,
P·P°C,CĤPēPjPeP° PSP°C,CĤC-CĤ
PiPSP°Cl̇P-C-PrPsPe CrC,PIPsCĤPμPSPSC‡
PSP°P±CĤCl̇PeC-PI, PiC-PrPiPēC%oPμPSPSC‡
PμPeCl̇PeCĤPμC†C-C— PeP°P»C-CĤ,
P±PμP·PrC-Cl̇P»CĤPSC-Cl̇C,Cḣ C,P°/P°P±Ps
P°C,CĤPsC,,C-Cl̇ PePsCĤPē
PSP°PrPSPēCĤPePsPiPēC... P·P°P»PsP·,
C‡PμCĤPiPsPSC- Cl̇C,CĤC-C—,
Cl̇C,PμCĤPsC—PrPSPμ P°PePSPμ,
PiPsCĤCrCēPμPSPSC‡ Cl̇PμPeCĤPμC†C-C—
Cl̇C,P°C,PμPiPēC... PiPsCĤPjPsPSC-PI
(PSP·PiCĤPēPeP°P°Pr P°PjPμPSPsCĤPμC‡,
C-PrCĤCrC,PēP·Pj, C-PjPiPsC,PμPSC†C-C‡)
P—P°C,CĤPēPjPeP° CĤPsCl̇C,Cr Cr
PrC-C,PμPNē
P°P»P°CrPePsPjP°, PeP°C,P°CĤP°PeC,P°,
PSPμC‡C-C,PePēPNē P·C-CĤ
P°PēCl̇PiPμPiCl̇C-C‡, P±C-P»Cḣ Cr
P¶PēPiPsC,C-
P°PēCĤP°P·PeP° CēP»CrPSPeCr P°P±Ps
PrPiP°PSP°PrC†C‡C,PēPiP°P»PsC—
PePēCēPePē
PμP°PSPeCĤPμP°C,PēC,
P—P°PiPsCĤ
PμC-PrPiPēC%oPμPSPSC‡ CĤPēP·PēPeCr
C-PSC,,PμPeC†C-PNē
P·C-P»Cḣ Cr PjᵼĤ™ Cl̇P·P°C... C,P°
Cl̇CrPiP»PsP±P°C..., PjᵼĤ™ Cl̇P·PsPiP°
Cl̇P»P°P±PeC-Cl̇C,Cḣ C,P°
PiPsCl̇PjPēPeCrPiP°PSPSC‡,
PsCl̇C,PμPsPiPsCĤPsP·
PhCl̇C,PμPsPSPμPeCĤPsP·
P°PsP»PsPiPSPēPNē P±C-P»Cḣ
PμCl̇PμPiPrPsPiCrC...P»PēPSP° PjPsP·PeCr P·
PSP°P±CĤCl̇PePsPj PsPiC,PēC‡PSPsPiPs
PrPēCl̇PeP° Cr PiC-PrP»C-C,PeC-PI
P°PμPiCĤPμCl̇C-C‡,
PrCĤP°C,C-PIP»PēPiC-Cl̇C,Cḣ,
PμPNēC,,PsCĤC-C‡
PμCl̇PēC...PsPjPsC,PsCĤPSP°
PiC-PiPμCĤP°PeC,PēPiPSC-Cl̇C,Cḣ,
C,CĤPēPiPsP¶PSC-Cl̇C,Cḣ
PhPiCĤPμCl̇C-C‡
PhP»PμCĤPiC-C‡PSP° PμPeP·P°PSC,PμPjP°,
PiPμC,PμC...C-C—,
CrPiPsPiC-P»CḣPSPμPSPSC‡
P·P°PiPsC°PSPSC‡ CĤP°PS,
PePsPSC,P°PeC,PSPēPNē PrPμCĤPjP°C,PēC,
P·PeC...C-PjPsP·
PμC-PrPiPēC%oPμPSPSC‡ CĤPēP·PēPeCr
C,CĤPsPjP±PsP·C-PI, PiP°Cl̇PeCrP»C-C,
(Cl̇PēPSP°PSPsPj PiC-PrPjC-PSPē PiC-Cl̇P»C‡
C,CĤPēPiP°P»PsC-C,C,PμCĤP°PiC-C—)
P·C,PsPiP°, PSPμP·PrCrP¶P°PSPSC‡

P'C-P»CHC€C-CÍ'C,CH PIPëC%oPµPIPëP°P·P°PSPëC... PïPsP±C-C±PSPëC... CĤPµP°PeC†C-PN₂,
C,P°PePsP¶ PjPsP¶PSP° PsC±C-PeCrPIP°C,Pë PiCĤPë P»C-PeCrPIP°PSPSC- C-PSC€PëPjPë
PiP»CĤPePsPePsCĤC,PëPePsCÍ'C,PµCĤPsC—PrP°PjPë.

P†PSPsPrC- PjPsP¶CrC,CH CÍ'PiPsCÍ'C,PµCĤC-PiP°C,PëCÍ'CH PïPsP±C-C±PSC- PµC,,PµPeC,Pë,
C,PëPiPsPIC- PrP»CĤ CÍ'PëCÍ'C,PµPjPSPëC... PiP»CĤPePsPePsCĤC,PëPePsC—PrC-PI. P|C-
PïPsP±C-C±PSC- CĤPµP°PeC†C-C— P·P°P»PµP¶P°C,CH PIC-Pr PrPsP·CrPIP°PSPSCĤ,
C,CĤPëPIP°P»PsCÍ'C,C- P»C-PeCrPIP°PSPSCĤ, PsPrPSPsC±P°CÍ'PSPsPiPs P°P±Ps
PïPsPiPµCĤPµPrPSCĤPsPiPs P»C-PeCrPIP°PSPSCĤ C-PSC€PëPjPë
PiP»CĤPePsPePsCĤC,PëPePsC—PrP°PjPë C,P° PIC-Pr C-PSPPrPëPIC-PrCrP°P»CHPSPsC—
C±CrC,P»PëPIPsCÍ'C,C-.

PµP»C-PSC-C±PSC- PrPsCÍ'P»C-PrP¶PµPSPSCĤ, PiCĤPsPIPµPrPµPSC- P·P° CrC±P°CÍ'C,CĤ
PiP°C†C-C''PSC,C-PI P· C...PIPsCĤPsP±PsCĤ PµCĤPsPSP°, PïPsPeP°P·P°P»Pë, C%oPs
C±P°CÍ'C,PsC,P° P°CÍ'PsC†C-PN₂PsPIP°PSPëC... C-P· PiP»CĤPePsPePsCĤC,PëPePsC—PrP°PjPë
PïPsP±C-C±PSPëC... PµC,,PµPeC,C-PI P'CrPrPµPSPsC,,P°P»CHPeCr 3 PjPi PSPëP¶C±P° PiCĤPë
PiPµCĤPsCĤP°P»CHPSPsPjCr PiCĤPëPN₂PsPjC- P±CrPrPµCÍ'PsPSC-PrCr, PSC-P¶ PiCĤPë
PiPµCĤPsCĤP°P»CHPSPsPjCr P·P°CÍ'C,PsCÍ'CrPIP°PSPSC- PµPePIC-PIP°P»PµPSC,PSPsC—
PrPsP·Pë PiCĤPµPrPSC-P·PsP»PsPSCr.

PµPsCÍ'PëP»PµPSPSCĤ P°P±Ps PïPsPIC,PsCĤPSP° PïPsCĤPIP° PïPsP·P°PePëC€PePsPIPëC...
PiCĤPsCĤPIC-PI (PsCÍ'PsP±P»PëPIPs PSP° C€PeC-CĤC- C,P° CÍ'CrPiP»PsP±P°C...)
PjPsP¶P»PëPIC- PiCĤPë PiPµCĤPµC...PsPrC- PiP°C†C-C''PSC,P° P· CÍ'PëCÍ'C,PµPjPSPëC...
PiP»CĤPePsPePsCĤC,PëPePsC—PrC-PI PSP° P±CrPrPµCÍ'PsPSC-Pr PjC-CÍ'C†PµPIPsC— PrC-C—.

*PµPsP±C-C±PSC- CĤPµP°PeC†C-C— PI CĤP°PjPeP°C... PeP»C-PSC-C±PSPëC...
PrPsCÍ'P»C-PrP¶PµPSCĤ C± PiPµPrC-P°C,CĤPëC±PSPëC... PiP°C†C-C''PSC,C-PI*

PI'PIPsCĤPsP±P° PµCĤPsPSP°

Pj PeP»C-PSC-C±PSPëC... PIPëPiCĤPsP±CrPIP°PSPSCĤC... PeP°PiCÍ'CrP»
P'CrPrPµPSPsC,,P°P»CHPeCr PïPs 3 PjPi Cr 82 PiPµPrC-P°C,CĤPëC±PSPëC... PiP°C†C-C''PSC,C-PI
P· C...PIPsCĤPsP±PsCĤ PµCĤPsPSP° PSP°PN₂C±P°CÍ'C,C-C€PëPjPë PSPµP±P°P¶P°PSPëPjPë
PµC,,PµPeC,P°PjPë P±CrP»Pë PiCĤPëPiPSC-C±PµPSPSCĤ PSP°PrPSPëCĤPePsPIPëC... P·P°P»PsP·
C,P° PiPsP»PsIPSPëPN₂ P±C-P»CH. PµPsPIC-PrPsPjP»CĤP»PsCÍ'CĤ PiCĤPs PïPsP±C-C±PSC-
PµC,,PµPeC,Pë, C...P°CĤP°PeC,PµCĤPSC- PrP»CĤ
PiP»CĤPePsPePsCĤC,PëPePsCÍ'C,PµCĤPsC—PrC-PI, P° C,P°PePsP¶ PiCĤPs C-PSC€C-
CĤC-PrPeC-CÍ'PSC- CĤPµP°PeC†C-C—, C,P°PeC- CĤPe P·P°PiP°PjPsCĤPsC±PµPSPSCĤ,
PSCrPrPsC,P°, P±P»CĤPIP°PSPSCĤ C,P° PiC-PiPµCĤP°PeCrCÍ'PëCÍ' (PrPëPI. CĤPsP·PrC-P»
B«PµP°CĤPjP°PePsP»PsPiC-C±PSC- PIP»P°CÍ'C,PëPIPsCÍ'C,C-B»).

PĤC±C,PsC-PjC±PSPSPëPN₂ PiPµPiP°C,PëC,

P''P°PSC- P· P±PµP·PiPµPePë PI PeP»C-PSC-C±PSPsPjCr PrPsCÍ'P»C-PrP¶PµPSPSC- P·P°
CrC±P°CÍ'C,CĤ 42 PiPµPrC-P°C,CĤPëC±PSPëC... PiP°C†C-C''PSC,C-PI P· P°CrC,PsC-PjCrPSPSPëPj
PiPµPiP°C,PëC,PsPj PiPsPeP°P·P°P»Pë, C%oPs PSPµP±P°P¶P°PSC- PµC,,PµPeC,Pë, PiCĤPs CĤPeC-
PïPsPIC-PrPsPjP»CĤP»PsCÍ'CĤ, PSPµ PIC-PrCĤC-P·PSCĤP»PëCÍ'CĤ C,P° PSPµ P±CrP»Pë
C±P°CÍ'C,C-C€PëPjPë, PSC-P¶ Cr PrPsCĤPsCÍ'P»PëC... Cr C†CHPsPjCr PrPsCÍ'P»C-PrP¶PµPSPSC-
(PrPëPI. CĤPsP·PrC-P» B«PµP°CĤPjP°PePsP»PsPiC-C±PSC- PIP»P°CÍ'C,PëPIPsCÍ'C,C-B»).

PŷPμCḡPjC-PS PīCḡPēPrP°C,PSPsCÍC,C-. 3 CḡPsPePē.

PḱPμ PjPsP¶PSP° P·P°CÍC,PsCÍPsPICrPIP°C,Pē PīC-CÍP»C¶ P·P°PeC-PSC‡PμPSPSC¶
C,PμCḡPjC-PSCr PīCḡPēPrP°C,PSPsCÍC,C-, P·P°P·PSP°C‡PμPSPsPiPs PSP° CrPīP°PePsPIC†C-.

PJPjPsPIPē P·P±PμCḡC-PiP°PSPSC¶. P—P±PμCḡC-PiP°C,Pē PīCḡPē C,PμPjPīPμCḡP°C,CrCḡC-
PSPμ PIPēC‰Pμ 25 B°PŸ. P—P±PμCḡC-PiP°C,Pē Cr PSPμPrPsCÍC,CrPīPSPsPjCr PrP»C¶
PrC-C,PμPNē PjC-CÍC†C-.

PJPīP°PePsPIPeP°. PμPs 10 PeP°PīCÍCrP» Cr P±P»C-CÍC,PμCḡC-, PīPs 5 P°P±Ps 10
P±P»C-CÍC,PμCḡC-PI Cr PePsCḡPsP±C†C- P· PeP°CḡC,PsPSCr.B B B B B B B

PḽP°C,PμPiPsCḡC-C¶ PIC-PrPīCrCÍPeCr. P—P° CḡPμC†PμPīC,PsPj.

P'PēCḡPsP±PSPēPe.

P"Ḥ. PαP°P»CHPe PαP°CḡPjP° P"PjP±PÍ, PḱC-PjPμC‡C‡PēPSP° / Dr. Falk Pharma GmbH,
Germany.

***PḥC-CÍC†PμP·PSP°C...PsPrP¶PμPSPSC¶ PIPēCḡPsP±PSPēPeP° C,P° P°PrCḡPμCÍP°
PjC-CÍC†C¶ PīCḡPsPIP°PrP¶PμPSPSC¶ PNēPsPiPs PrC-C¶P»CHPSPsCÍC,C-.***

P>C¶PNēPSPμPSPIPμP±PμCḡC€C,CḡP°CÍCÍPμ 5, 79108 PαCḡP°PNēP±CrCḡPi P†Pj
P'ḤP°PNēCÍPiP°Cr, PḱC-PjPμC‡C‡PēPSP° / Leinenweberstrasse 5, 79108 Freiburg Im Breisgau,
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