

Р†РќРЎРЎР РЈРЉР†Р†РЇ

**РrР»CП РjРµРrРёC‡PSPsPiPs Р•Р°CЃC,PsCЃCѓPIР°PSPSCП Р»C-РёР°CЃCЃCРёPsPiPs
Р•Р°CЃCРsР±CЃ**

Р”РЈРћР”РћР РЎ

В (DUODARTВ„Ў)

РЎРёР»Р°Рr:

*РrC-CЃC‡C- CЃРµC‡PsPIPёPSPё: РrCЃC,Р°CЃC,РµCЃРёРr, C,Р°РјCЃCѓР»PsРёPSCЃ
PiC-РrCЃPsC...Р»PsCЃРёРr;*

1 РёР°РёCЃCѓР»Р° РјC-CЃC,РёC,ЧР РrCЃC,Р°CЃC,РµCЃРёРrCЃ 0,5 РјPi C,Р°
C,Р°РјCЃCѓР»PsРёPSCЃ PiC-РrCЃPsC...Р»PsCЃРёРrCЃ 0,4 РјPi;

***РrPsPiPsРјC-Р¶PSC- CЃРµC‡PsPIPёPSPё: РјPsPSPsРrРёPiР»C-C‡РµCЃРёРrРё
РёРёCЃР»PsC,Рё РёР°РёCЃРёР»PsPIPс—,
Р±CЃC,РёР»PiC-РrCЃPsРёCЃРёC,PsР»CЃPsР» (Р• 321), Р¶РµР»Р»Р°Р°Р°C,РёPS,
PiР»C-C‡РµCЃРёPS, C,РёC,Р°PSCЃ РrC-PsРёCЃРёРr (Р• 171), Р•Р°Р»C-Р•Р°
PsРёCЃРёРr Р¶PsPIC,РёPNё (Р• 172), C,CЃРёPiР»C-C‡РµCЃРёРrРё
CЃРµCЃРµРrPSCРёPsPiPs Р»Р°PSC‡CРёР° C,Р° Р»РµC‡РёC,РёPS;
C‡РµР»CЃР»PsР•Р° РјC-РёCЃPsРёCЃРёCЃC,Р°Р»C-С‡PSP°,
РјРµC,Р°РёCЃРёР»Р°C,Р°PSPsPiPs CЃPsPiPsР»C-РјРµCЃCЃ РrРёCЃРёРµCЃCЃC-СП,
C,Р°Р»CРё, C,CЃРёРµC,РёР»C‡РёC,CЃР°C,;***

***PsР±PsР»PsPSPёР C,PIРµCЃРrPsC— РёР°РёCЃCЃР»Рё: РёР°CЃР°PiC-PSP°PS
(Р• 407), РёР°Р»C-СР С...Р»PsCЃРёРr, C,РёC,Р°PSCЃ РrC-PsРёCЃРёРr (Р• 171),
FD&C Yellow 6 (E 110), PiC-PiCЃPsРјР»PsР°, PIC-CЃРё
РёР°CЃPSP°CЃCЃCРёРёPNё, РёCЃPsC...РјР°Р»CРё
РёCЃРёCЃCЃРrР•CПSPёPNё, Р•Р°Р»C-Р•Р° PsРёCЃРёРr C‡РµCЃPIPsPSPёPNё (Р•
172), SW-9008 Black Ink (СРµРµР°Р°Рё, PiCЃPsPiC-Р»РµPSPiР»C-РёPsР»CРё,
Р•Р°Р»C-Р•Р° PsРёCЃРёРr C‡PsCЃPSPёPNё (Р• 172), РёР°Р»C-СР
PiC-РrCЃPsРёCЃРёРr).***

Р»C-РёР°CЃCЃCРёР° C„PsCЃРјР°. РёР°РёCЃCЃР»Рё C,PIРµCЃРrC—.

РћCЃPSPsPIPsC- C„C-РёРёРёPs-C...C-РјC-С‡PSC- PIP»Р°CЃC,РёPIPsCЃC,C-: C,PIРµCЃРrР°

$P^{\circ}CrC, P^{\circ}ClC, P_{\mu}C_{\eta}P_{\delta}Pr$ $PiC_{\eta}P_{\delta}PiPSC-C\ddagger CrC$ ” $P^{\circ}PeC, P_{\delta}PiPSC-ClC, CH_3$ $ClPe$ 1- $PiPs$, $C, P^{\circ}Pe$ C- 2-
 $PiPs$ $C, P_{\delta}PiCr$ C- $P\cdot PsC$, „ $P_{\mu}C_{\eta}PjP_{\mu}PSC, C-PI$ 5- $P^{\circ}P$ » CH_3C „, $P^{\circ}-C_{\eta}P_{\mu}PrCrPeC, P^{\circ}P\cdot P_{\delta}$, $ClPeC-$
 $PIC-PrPiPsPIC-PrP^{\circ}CH_3C, CH_3$ $P\cdot P^{\circ}$ $PiP_{\mu}C_{\eta}P_{\mu}C, PIPsC_{\eta}P_{\mu}PSPSC_{\eta}$ $C, P_{\mu}ClC, PsClC, P_{\mu}C_{\eta}PsPSCr$
 PSP° $PrP_{\delta}PiC-PrC_{\eta}PsC, P_{\mu}ClC, PsClC, P_{\mu}C_{\eta}PsPS$ ($P^{\circ}P^{\circ}P_{\delta}$). $P^{\circ}P^{\circ}P_{\delta}C$ ” $P^{\circ}PSPrC_{\eta}PsPiP_{\mu}PSPsPj,$
 $ClPeP_{\delta}PN_{\delta}$ PI $PiP_{\mu}C_{\eta}C\ddagger Cr$ $C\ddagger P_{\mu}C_{\eta}PiCr$ $PIC-PrPiPsPIC-PrP^{\circ}C$ ” $P\cdot P^{\circ}$ $C_{\eta}C-ClC,$
 $PiP_{\mu}C_{\eta}P_{\mu}PrPjC-C...CrC_{\eta}PsPIPSC—$ $P\cdot P^{\circ}P$ » $PsP\cdot P_{\delta}$ C- $C_{\eta}PsP\cdot PIP_{\delta}C, PsPe$
 $PrPsP\pm C_{\eta}PsClPeC-ClPSPSC—$ $PiC-PiP_{\mu}C_{\eta}PiP$ » $P^{\circ}P\cdot C-C—$ $PiP_{\mu}C_{\eta}P_{\mu}PrPjC-C...CrC_{\eta}PsPIPSC—$
 $P\cdot P^{\circ}P$ » $PsP\cdot P_{\delta}$. $P_{\delta}P^{\circ}PjClCrP$ » $PsP\cdot P_{\delta}PS$ $PiC_{\eta}P_{\delta}PiPSC-C\ddagger CrC$ ” $P^{\circ}PeC, P_{\delta}PiPSC-ClC, CH_3$
 $P^{\circ}PrC_{\eta}P_{\mu}PSPsC_{\eta}P_{\mu}C\ddagger P_{\mu}PiC, PsC_{\eta}C-PI$ α_{1p} C- α_{1d} Cr $ClC, C_{\eta}PsPjP^{\circ}P$ » $CH_3PSC-PN_{\delta}$ PiP » $P^{\circ}PrPeC-PN_{\delta}$
 $PjCrClPeCrP$ » $P^{\circ}C, CrC_{\eta}C-$ $PiP_{\mu}C_{\eta}P_{\mu}PrPjC-C...CrC_{\eta}PsPIPSC—$ $P\cdot P^{\circ}P$ » $PsP\cdot P_{\delta}$ C- $C\ddagger P_{\delta}PN_{\delta}C\ddagger C-$

СГРµС±PSPiPs PjC-C...CpCП°. PµCПP±P»PëP·PSPs 75 % CПPµC†PµPïC,PsCПC-PI α₁ Cг PïPµCПPµPrPjC-C...CpCПPsPIC-PNë P·P°P»PsP·C- C” CПPµC†PµPïC,PsCПP°PjPë PïC-PrC,PëPïCг α₁P°.

PÿP°PjCГCзP»PsP·PëPS

PÿP°PjCГCгP»PsP·PëPS PïC-PrPIPëC%оCгC” PjP°PeCГPëPjP°P»CHBPCГ C€PIPëPrPeC-CГC,CH C,PsPeCг CГPµC±C- P·P° CПP°C...CгPSPsPe P·PSPëP¶PµPSPSCЦ C,PsPSCгCГCг PïP»P°PrPePëC... Pj'CЦP·C-PI CгCПPµC,CПPë C- PïPµCПPµPrPjC-C...CpCПPsPIPsC— P·P°P»PsP·Pë, C%оPs CгCГCгPIP°C” PsP±CГC,CПCгPeC†C-CH. PµCПPµPïP°CПP°C, C,P°PePsP¶ P·PSPëP¶CгC” PIPëCПP°P¶PµPSC-CГC,CH CГPëPjPïC,PsPjC-PI PïPsPrCПP°P·PSPµPSPSCЦ C,P° PsP±CГC,CПCгPeC†C-C—, Cг CПPsP·PIPëC,PeCг CЦPePëC... C-CГC,PsC,PSCг CПPsP»CH PIC-PrC-PiCПP°C” PSPµC,CПPëPjP°PSPSCЦ CГPµC±C- C,P° CГPePsCПPsC±PµPSPSCЦ PïP»P°PrPePëC... PjBП™ CЦP·C-PI PSPëP¶PSC-C... PIC-PrPrC-P»C-PI CГPµC±PSPiPIC-PrPSPëC... C€P»CЦC...C-PI. PÿP°PePëPNë PµC,,PµPeC, PrPsCГCЦPiP°C”C,CHCГCЦ PïC-Pr C±P°CГ PrPsPIPiPsC,CПPëPIP°P»PsC— C,PµCПP°PïC-C—. PкPµPsP±C...C-PrPSC-CГC,CH PsPïPµCПP°C,PëPIPSPsPiPs PIC,CПCгC±P°PSPSCЦ P°P±Ps PeP°C,PµC,PµCПPëP·P°C†C-C— P·PSP°C±PSPs P·PSPëP¶CгC”C,CHCГCЦ.

PПPSC,P°PiPsPSC-CГC,Pë α₁-P°PrCПPµPSPsCПPµC†PµPïC,PsCПC-PI PjPsP¶CгC,CH P·PjPµPSC€CгPIP°C,Pë PeCПPsIвП™ CЦPSPëPNë C,PëCГPe C€P»CЦC...PsPj P·PSPëP¶PµPSPSCЦ P·P°PiP°P»CHBSPsPiPs PïPµCПPëC,,PµCПPëC±PSPsPiPs PsPïPsCПCг. PµC-Pr C±P°CГ PrPsCГP»C-PrP¶PµPSPSCЦ PIPïP»PëPICг C,P°PjCГCгP»PsP·PëPSCг PSPµ CГPiPsCГC,PµCПC-PiP°P»PsCГCH PeP»C-PSC-C±PSPs P·PSP°C±CгC%оPsPiPs P·PSPëP¶PµPSPSCЦ PeCПPsIвП™ CЦPSPsPiPs C,PëCГPeCг.

PαP°CПPjP°PePsPeC-PSPµC,PëPeP°.

PПC-P¶ PIPiPµPrPµPSPSCЦPj PePsPjP±C-PSP°C†C-C— PrCгC,P°CГC,PµCПPëPr- C,P°PjCГCгP»PsP·PëPS C- PsPrPSPsC±P°CГPSPëPj PIPiPµPrPµPSPSCЦPj PrPsP· PrCгC,P°CГC,PµCПPëPrCг C- C,P°PjCГCгP»PsP·PëPSCг PI PeP°PïCГCгP»P°C... PsPeCПPµPjPs P±CгP»P° PïCПPsPrPµPjPsPSCГC,CПPsPIP°PSP° P±C-PsPµPePIC-PIP°P»PµPSC,PSC-CГC,CH.

P”PsCГP»C-PrP¶PµPSPSCЦ P±C-PsPµPePIC-PIP°P»PµPSC,PSPsCГC,C- PsPrPSPsCПP°P·PsPIPëC... PrPsP· P±CгP»Ps PïCПPsPIPµPrPµPSPs CЦPe PSP°C,C%оPµ, C,P°Pe C- PïC-CГP»CЦ PïCПPëPNëPsPjCг C—P¶C-. Pj PïPsCПC-PIPSCЦPSPSC- P·C- CГC,P°PSPsPj PSP°C,C%оPµ, Cг CПP°P·C- P·P°CГC,PsCГCгPIP°PSPSCЦ PïC-CГP»CЦ PïCПPëPNëPsPjCг C—P¶C- CГPiPsCГC,PµCПC-PiP°P»PsCГCЦ 30 % P·PSPëP¶PµPSPSCЦ C_{max} (PjP°PeCГPëPjP°P»CHBSPsC— PePsPSC†PµPSC,CПP°C†C-C—) C,P°PjCГCгP»PsP·PëPSCг Cг CГPeP»P°PrC- PePsPjP±C-PSP°C†C-C— PrCгC,P°CГC,PµCПPëPr-C,P°PjCГCгP»PsP·PëPS. P±P¶P° PSPµ PIPïP»PëPIP°P»P° PSP° AUC (PïP»PsC%оCг PïC-Pr C,,P°CПPjP°PePsPeC-PSPµC,PëC±PSPsCП PeCПPëPIPsCH) C,P°PjCГCгP»PsP·PëPSCг.

P’CГPjPsPeC,CзPIP°PSPSCЦ

P”CгC,P°CГC,PµCПPëPr

PµC-CГP»CЦ PïPµCПPsCПP°P»CHBSPsPiPs PIPiPµPrPµPSPSCЦ PsPrPSPsCПP°P·PsPIPsC— PrPsP·Pë 0,5 PjPi PrCгC,P°CГC,PµCПPëPrCг C±P°CГ PrPs PrPsCГCЦPiPSPµPSPSCЦ PNëPsPiPs

$$\text{Pj} \cdot \text{C} \ddagger \text{PsP} \gg \text{PsPIC} - \text{PeC} - \text{PI} \cdot \text{C}, \text{P}^\circ \text{Pj} \text{C} \dot{\text{I}} \text{C} \dot{\text{r}} \text{P} \gg \text{PsP} \cdot \text{P} \ddot{\text{e}} \text{PS} \cdot \text{P} \cdot \text{PI} \text{B} \text{H}^{\text{TM}} \text{C} \dot{\text{I}} \text{P} \cdot \text{C} \dot{\text{r}} \text{C}'' \text{C}, \text{C} \text{H} \text{C} \dot{\text{I}} \text{C} \dot{\text{I}} \text{P} \cdot \text{P} \pm \text{C} - \text{P} \gg \text{PeP}^\circ \text{Pj} \text{P} \ddot{\text{e}}$$

PiP»P°P·PjPë PiCTjPëP±P»PëP·PSPs PSP° 99 %. PhP±Bj™ C”Pj CTjPsP·PiPsPrC-P»Cr C”
PSPµPIPµP»PëPePëPj (PiCTjPëP±P»PëP·PSPs 0,21/PePi).

PhPµC, P°P±PsP»C-P·Pj

P”CrC, P°CrC, PµCTjPëPr

P”CrC, P°CrC, PµCTjPëPr P°PeC, PëPIPSPs PjPµC, P°P±PsP»C-P·CrC”C, CHCrCj in vivo. P’
CrPjPsPIP°C... in vitro PrCrC, P°CrC, PµCTjPëPr PjPµC, P°P±PsP»C-P·CrC”C, CHCrCj
C†PëC, PsC...CTjPsPjPsPjB P450 3A4 C- 3A5, CrC, PIPsCTjCTjCTjC†Pë C, CTjPë
PjPsPSPsPiC-PrCTjPsPeCrPëP»CHPsPIP°PSPëC... PjPµC, P°P±PsP»C-C, Pë C- PsPrPëPS
PrPëPiC-PrCTjPsPecPëP»CHPsPIP°PSPëPNë PjPµC, P°P±PsP»C-C,.

PµC-CrP»Cj PiPµCTjPsCTjP°P»CHPsPSPsPiPs PIPiPµPrPµPSPSCj PrCrC, P°CrC, PµCTjPëPrCr PI
PrPsP·C- 0,5 PjPi/PrPsP±Cr PrPs PrPsCrCjPiPSPµPSPSCj CTjC-PIPSPsPIP°P¶PSPsC—
PePsPSC†PµPSC, CTjP°C†C-C— 1,0Bj”15,4 % (CrPµCTjPµPrPSC” P·PSP°C†PµPSPSCj Bj” 5,4 %)
PIPiPµPrPµPSPsC— PrPsP·Pë PrCrC, P°CrC, PµCTjPëPrCr PIPëPrC-P»CjC”C, CHCrCj Cr PeP°P»
CrB PSPµP·PjC-PSPµPSPsPjCrB PIPëPiP»CjPrC-.B P PµC€C, P° PIPëPrC-P»CjC”C, CHCrCj Cr
PeP°P» Cr PIPëPiP»CjPrC- 4 PsCrPSPsPIPSPëC... PjPµC, P°P±PsP»C-C, C-PI, C%oPs
PjC-CrC, CjC, CH 39 %, 21 %, 7 % C- 7 % PePsP¶PSPsC— P· CTjPµC†PsPIPëPS,
PiPsPiBj™ CjP·P°PSPëC... P· P»C-PeP°CTjCrCHPePëPj P·P°CrPsP±PsPj, C- 6
PrCTjCrPiPsCTjCjPrPSPëC... PjPµC, P°P±PsP»C-C, C-PI (PjPµPSC€Pµ 5 % PePsP¶PµPS). Pj
CrPµC†C- P»CHPrPëPSPë PIPëCjPIP»PµPSPs P»PëC€Pµ PSPµP·PSP°C†PSC-
PeC-P»CHPePsCrC, C- PSPµP·PjC-PSPµPSPsPiPs PrCrC, P°CrC, PµCTjPëPrCr (PjPµPSC€Pµ PSC-P¶
0,1 % PrPsP·Pë).

PjP°PjCrCrP»PsP·PëPS

P·PSP°PSC, C-PsPjPµCTjPSP° P±C-PsPePsPSPIPµCTjCrC-Cj P· C, P°PjCrCrP»PsP·PëPSCr
PiC-PrCTjPsC...P»PsCTjPëPrCr [R(-) C-P·PsPjPµCTj] Cr S() C-P·PsPjPµCTj Cr P»CHPrPëPSPë PSPµ
PIC-PrP±CrPIP°C”C, CHCrCj. PjP°PjCrCrP»PsP·PëPSCr PiC-PrCTjPsC...P»PsCTjPëPr
P°PeC, PëPIPSPs PjPµC, P°P±PsP»C-P·CrC”C, CHCrCj C,, PµCTjPjPµPSC, P°PjPë
C†PëC, PsC...CTjPsPjCr P450 Cr PiPµC†C-PSC†C-, C- PjPµPSC€Pµ 10 % PrPsP·Pë
PIPëPrC-P»CjC”C, CHCrCj Cr CrPµC†Cr PI PSPµP·PjC-PSPµPSPsPjCr PIPëPiP»CjPrC-. PhP»Pµ
C,, P°CTjPjP°PePsPeC-PSPµC, PëC†PSPëPNë PiCTjPsC,, C-P»CH PjPµC, P°P±PsP»C-C, C-PI Cr
P»CHPrPëPSPë PSPµ PICrC, P°PSPsPIP»PµPSPëPNë. P PµP·CrP»CHC, P°C, Pë
PrPsCrP»C-PrP¶PµPSCH in vitro PIPeP°P·CrCTjC, CH PSP° C, Pµ, C%oPs PrPs
PjPµC, P°P±PsP»C-P·PjCr C, P°PjCrCrP»PsP·PëPSCr P·P°P»CrC†P°CTjC, CHCrCj
C,, PµCTjPjPµPSC, Pë CYP3A4 C- CYP2D6, P° C, P°PePsP¶ PSPµP·PSP°C†PSPsCTj C” CrC†P°CrC, CH
C-PSC€PëC... C-P·PsC,, PµCTjPjPµPSC, C-PI CYP.

PµCTjPëPiPSC-C†PµPSPSCj P°PeC, PëPIPSPsCrC, C- C,, PµCTjPjPµPSC, C-PI, CjPeC-
P±PµCTjCrC, CH CrC†P°CrC, CH Cr PiPµC†C-PSPePsPIPsPjCr PjPµC, P°P±PsP»C-P·PjC-, PjPsP¶Pµ
PiCTjPëP·PIPµCrC, Pë PrPs PiPsCrPëP»PµPSPsC— PrC-C— C, P°PjCrCrP»PsP·PëPSCr. PµPµCTjPµPr
PIPëPIPµPrPµPSPSCjPj P· CrPµC†PµCTj PjPµC, P°P±PsP»C-C, Pë C, P°PjCrCrP»PsP·PëPSCr
PiC-PrCTjPsC...P»PsCTjPëPrCr PiC-PrPrP°CTjC, CHCrCj C€PëCTjPsPePsPjCr
P·PiBj™ CjP·CrPIP°PSPSCr P· PiP»CHPeCrCTjPsPSC-PrPsPj P°P±Ps CrCrP»CHC,, P°C, PsPj.

P’PëPIPµPrPµPSPSCj

P”CrC, P°CrC, PµCTjPëPr

P’PëPIPµPrPµPSPSCj PrCrC, P°CrC, PµCTjPëPrCr P·P°P»PµP¶PëC, CH PIC-Pr PrPsP·Pë, C-

C†PμPNε PιCΉPsC†PμCΓ CΓP»C-Pr PsPιPεCΓCρPIP°C,Pε C΀Pε C,P°PePεPNε, C%Ps
PIC-PrP±CρPIP°C”C,CHCΓC΀ PrPIPsPjP° PιP°CΉP°P»PμP»CHΉPSPεPjPε CεP»C΀C...P°PjPε:
PsPrPεPS C” PSP°CΓPεC†CρPIP°PSPεPj PιCΉPε PeP»C-PSC-C†PSPs P·PSP°C†CρC%PεC...
PePsPSC†PμPSC,CΉP°C†C-C΀C..., P° PrCΉCρPiPεPNε BΉ” PSPμPSP°CΓPεC†CρPIP°PSPεPj. PμCΉPε
PSPεP·CHΉPePεC... PePsPSC†PμPSC,CΉP°C†C-C΀C... Cρ CΓPεCΉPsPIP°C,C†C- PeCΉPsPIC-
(PjPμPSCεPμ 3 PSPI/PjP») PrCρC,P°CΓC,PμCΉPεPr CεPIPεPrPePs PIPεPIPsPrPεC,CHCΓC΀ C΀Pε
P·P°P»PμP¶PSPεPj PIC-Pr PePsPSC†PμPSC,CΉP°C†C-C—, C,P°Pe C- PSPμP·P°P»PμP¶PSPεPj
PIC-Pr PePsPSC†PμPSC,CΉP°C†C-C— CεP»C΀C...PsPj. PμCΉPε P·P°CΓC,PsCΓCρPIP°PSPSC-
PsPrPSPsCΉP°P·PsPIPεC... PrPsP· 5 PjPi P°P±Ps PjPμPSCεPεC... PrPsP· P±CρP»Ps
PIPεC΀PIP»PμPSPs PsP·PSP°PePε CεPIPεPrPePsPiPs PeP»C-CΉPμPSCΓCρ C-
PICΓC,P°PSPsPIP»PμPSPs PιPμCΉC-PsPr PSP°PιC-PIPIPεPIPμPrPμPSPSC΀, C΀PεPεPNε
C,CΉPεPIP°C” PIC-Pr 3 PrPs 9 PrPSC-PI.

PμCΉPε C,PμCΉP°PιPμPIC,PεC†PSPεC... PePsPSC†PμPSC,CΉP°C†C-C΀C... PιC-CΓP»C΀
PιPsPIC,PsCΉPSPsPiPs PIPIPμPrPμPSPSC΀ PrPsP·Pε 0,5 PjPi/PrPsP±Cρ PrPsPjC-PSCΓC”
PιPsPIC-P»CHΉPSC-CεPεPNε, P»C-PSC-PNεPSPεPNε CεP»C΀C... PIPεPIPμPrPμPSPSC΀, P°
PιPμCΉC-PsPr PSP°PιC-PIPIPεPIPμPrPμPSPSC΀ CΓC,P°PSPsPIPεC,CH PιCΉPεP±P»PεP·PSPs
3BΉ”5 C,PεP¶PSC-PI.

PϣP°PjCΓCρP»PsP·PεPS

PϣP°PjCΓCρP»PsP·PεPS C- PNεPsPiPs PjPμC,P°P±PsP»C-C,Pε PIPεPIPsPrC΀C,CHCΓC΀
PιPμCΉPμPIP°P¶PSPs P· CΓPμC†PμCΉ, PI C΀PεC-PNε PιCΉPεP±P»PεP·PSPs 9 % PrPsP·Pε
PιCΉPεCΓCρC,PSC- Cρ PIPεPiP»C΀PrC- PSPμP·PjC-PSPμPSPsC— P°PeC,PεPIPSsC—
CΉPμC†PsPIPεPSPε.

PμC-CΓP»C΀ PIPSCρC,CΉC-CεPSCΉPsPIPμPSPSPsPiPs P°P±Ps PιPμCΉPsCΉP°P»CHΉPSPsPiPs
PIPIPμPrPμPSPSC΀ PI P»C-PeP°CΉCΓCHΉPeC-PNε C,,PsCΉPjC- P· PSPμPiP°PNεPSPεPj
PIPεPIC-P»CHΉPSPμPSPSC΀Pj PιPμCΉC-PsPr PSP°PιC-PIPIPεPIPμPrPμPSPSC΀
C,P°PjCΓCρP»PsP·PεPSCρ, C%Ps PjC-CΓC,PεC,CHCΓC΀ Cρ PιP»P°P·PjC- PeCΉPsPIC-,
PePsP»PεPIP°C”C,CHCΓC΀ PI PrC-P°PιP°P·PsPSC- PIC-Pr 5 PrPs 7 PiPsPrPεPS. P\$PμCΉPμP·
C,,P°CΉPjP°PePsPeC-PSPμC,PεPeCρ, CΉPμPiCρP»CHΉPsPIP°PSCρ CεPIPεPrPeC-CΓC,CH
PιPsPiP»PεPSP°PSPSC΀, Cρ PIPεPιP°PrPeCρ P· C,P°PjCΓCρP»PsP·PεPSPsPj Cρ PeP°PιCΓCρP»P°C...
P· PjPsPrPεC,,C-PePsPIP°PSPεPj PIPεPIC-P»CHΉPSPμPSPSC΀Pj, CΓPιCΉP°PIP¶PSC-PNε
PιPμCΉC-PsPr PSP°PιC-PIPIPεPIPμPrPμPSPSC΀ C,P°PjCΓCρP»PsP·PεPSCρ,
PιCΉPεPNεPSC΀C,PsPiPs PιC-CΓP»C΀ C—PrPε, CΓC,P°PSPsPIPεC,CH PιCΉPεP±P»PεP·PSPs 10
PiPsPrPεPS, P° PI CΉC-PIPSsPIP°P¶PSC-PNε PePsPSC†PμPSC,CΉP°C†C-C— Cρ
PιP°C†C-C”PSC,C-PI BΉ” PιCΉPεP±P»PεP·PSPs 13 PiPsPrPεPS.

PμP°C†C-C”PSC,Pε P»C-C,PSCHΉPsPiPs PIC-PeCé

P”CρC,P°CΓC,PμCΉPεPr

PμP°CΉPjP°PePsPeC-PSPμC,PεPeP° PrCρC,P°CΓC,PμCΉPεPrCρ PsC†C-PSCΉPIP°P»P°CΓC΀ Cρ 36
P·PrPsCΉPsPIPεC... C†PsP»PsPIC-PeC-PI Cρ PIC-C†C- PIC-Pr 24 PrPs 87 CΉPsPeC-PI PιC-CΓP»C΀
PIPIPμPrPμPSPSC΀ PsPrPSPsCΉP°P·PsPIPsC— PrPsP·Pε 5 PjPi. P—PSP°C†PSPsC—
P·P°P»PμP¶PSPsCΓC,C- PIPιP»PεPICρ PrCρC,P°CΓC,PμCΉPεPrCρ PIC-Pr PIC-PeCρ
PιP°C†C-C”PSC,P° PSPμ CΓPιPsCΓC,PμCΉC-PιP°P»PsCΓC΀, P°P»Pμ PιPμCΉC-PsPr
PSP°PιC-PIPIPεPIPμPrPμPSPSC΀ P±CρPI PePsCΉPsC,CεPεPj Cρ C†PsP»PsPIC-PeC-PI PIC-PePsPj
PrPs 50 CΉPsPeC-PI. PϣC,P°C,PεCΓC,PεC†PSPεC... PIC-PrPjC-PSPSPsCΓC,PμPNε Cρ
PιPμCΉC-PsPrC- PSP°PιC-PIPIPεPIPμPrPμPSPSC΀ PSPμ P±CρP»Ps PιCΉPε
PιPsCΉC-PIPSC΀PSPSC- PιCΉCρPιPε 50BΉ”69-CΉC-C†PSPεC... PrPsCΓP»C-PrP¶CρPIP°PSPεC... P·

PiC₇Cr₇PiPsC₇ PrPsC₇P»C-PrP₇Cr₇PIP°PSPëC... PIC-PePsPj PiPsPSP°Pr 70 C₇PsPeC-PI.

PÿP°PjC₇Cr₇P»PsP·PëPS

P₇P₇C₇P₇C...C₇P₇C₇PSP₇ PiPsC₇C-PIPSC₇IP»CH₇PSP₇ PrPsC₇P»C-PrP₇P₇PSPSC₇ P·P°PiP°P»CH₇PSPsPiPs PIP°P»PëPIC₇ C,P°PjC₇Cr₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇ (AUC (PiP»PsC%₀C- PiC-Pr C,,P°C₇PjP°PePsPeC-PSP₇C,PëC₇PSPsC₇ PeC₇PëPIPsC₇)) C- P₇P₇C₇C-PsPrC₇ PSP°PiC-PIPIPëPIP₇PrP₇PSPSC₇ PIPeP°P·C₇C" PSP° C,P₇, C%₀Ps C,,P°C₇PjP°PePsPeC-PSP₇C,PëC₇PSP° PrC-C₇ C,P°PjC₇Cr₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇ PjPsP₇P₇ P±C₇C,Pë C,C₇PsC...Pë C,C₇PëPIP°P»C-C₇PsC₇ Cr PIP°C₇C-C"PS₇C,PI P»C-C,PSC₇PsPiPs PIC-PeC₇ PiPsC₇C-PIPSC₇IPSPs P· PjPsP»PsPrPëPjPë P·PrPsC₇PsPIPëPjPë PrPsP±C₇PsPIPsP»CH₇C₇IPjPë C₇PsP»PsPIC-C₇PsC— C₇C,P°C,C-. P'P»P°C₇PSPëPN₇ PeP»C-C₇P₇PSC₇ PSP₇ P·P°P»P₇P₇PëC,CH₇ PIC-Pr P·PIB₇TM C₇IP·C₇PIP°PSPSC₇ C,P°PjC₇Cr₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇ P· P°P»CH₇C,,P°-1-PePëC₇P»PëPj PiP»C-PePsPiC₇PsC,P₇C—PSPsPj, P°P»P₇ P·PSPëP₇Cr₇C"CH₇C₇ C₇ P· PIC-PePsPj PiP°C₇C-C"PS₇C,P°, Cr C₇P₇P·C₇P»CH₇C,P°C,C- C₇PsPiPs P·P°PiP°P»CH₇PSP° PrC-C₇ C" PSP° 40 % C₇PëP»CH₇PSC-C₇PsC₇ (AUC) Cr PiP°C₇C-C"PS₇C,PI PIC-PePsPj PIC-Pr 55 PrPs 75 C₇PsPeC-PIB PiPsC₇C-PIPSC₇IPSPs P· PrC-C"CH₇ Cr PIP°C₇C-C"PS₇C,PI PIC-PePsPjB 20B₇"32 C₇PsPePë.

P₇PëC₇PePsPIP° PSP₇PrPsC₇C,P°C,PSC-C₇C,CH

P"Cr₇C,P°C₇C,P₇C₇PëPr

P'PiP»PëPI PSPëC₇PePsPIPsC— PSP₇PrPsC₇C,P°C,PSPsC₇C,C- PSP° C,,P°C₇PjP°PePsPeC-PSP₇C,PëPeC₇ PrC₇C,P°C₇C,P₇C₇PëPrC₇ PSP₇ PIPëPIC₇P°P»Pë. P₇P»P₇ Cr C₇P₇C₇C- P»CH₇PrPëPSPë PIPëC₇IP»C₇C"CH₇C₇ PjP₇PSC₇P₇ 0,1 % PrPsP·Pë PrC₇C,P°C₇C,P₇C₇PëPrC₇ 0,5 PjPi Cr C₇C-PIPS₇PIP°P₇PSC-PN₇ PePsPSC₇P₇PSC,C₇P°C₇C-C—, C,PsPjCr PeP»C-PSC-C₇PSPs P·PSP°C₇C₇C%₀PsPiPs PiC-PrPIPëC%₀P₇PSPSC₇ PePsPSC₇P₇PSC,C₇P°C₇C-C— PrC₇C,P°C₇C,P₇C₇PëPrC₇ Cr PiP»P°P·PjC- PeC₇PsPIC- Cr PIP°C₇C-C"PS₇C,PI P· PSPëC₇PePsPIPsC₇ PSP₇PrPsC₇C,P°C,PSC-C₇C,CH₇ PsC₇C-PeC₇PIP°C,Pë PSP₇ C₇P»C-PrB (PrPëPI. C₇PsP·PrC-P» B«PÿPiPsC₇C-P± P·P°C₇C,PsC₇Cr₇PIP°PSPSC₇ C,P° PrPsP·PëB»).

PÿP°PjC₇Cr₇P»PsP·PëPS

P₇P°C₇PjP°PePsPeC-PSP₇C,PëPeP° C,P°PjC₇Cr₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇ PiPsC₇C-PIPSC₇PIP°P»P°C₇C₇ Cr 6 PIP°C₇C-C"PS₇C,PI P· PSPëC₇PePsPIPsC₇ PSP₇PrPsC₇C,P°C,PSC-C₇C,CH₇ PIC-Pr C₇P»P°P±PePsPiPs PrPs PiPsPjC-C₇PSPsPiPs (30 ≤ CL_{cr} < 70 PjP»/C...PI/1,73 Pj²) P°P±Ps PIC-Pr PiPsPjC-C₇PSPsPiPs PrPs C,C₇IP₇PePsPiPs (10 ≤ CL_{cr} < 30 PjP»/C...PI/1,73 Pj²) C₇C,CrPiP₇PSC₇ C- Cr 6 PrPsC₇P»C-PrP₇Cr₇PIP°PSPëC... P· PSPsC₇PjP°P»CH₇PSPëPj PeP»C-C₇P₇PSC₇P₇Pj (CL_{cr} < 90 PjP»/C...PI/1,73 Pj²). Pj C,PsPN₇ C₇P°C₇ C₇IPe Cr P·P°PiP°P»CH₇PSC-PN₇ PePsPSC₇P₇PSC,C₇P°C₇C-C— C,P°PjC₇Cr₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇ Cr PiP»P°P·PjC- PeC₇PsPIC- C₇PiPsC₇C,P₇C₇C-PiP°P»P°C₇C₇ P·PjC-PSP° PI C₇P₇P·C₇P»CH₇C,P°C,C- P·PjC-PSPSPsPiPs P·PIB₇TM C₇IP·C₇PIP°PSPSC₇ P· P°P»CH₇C,,P°-1-PePëC₇P»PëPj PiP»C-PePsPiC₇PsC,P₇C—PSPsPj, PePsPSC₇P₇PSC,C₇P°C₇C-C₇ PSP₇P·PIB₇TM C₇IP·P°PSPsPiPs (P°PeC,PëPIPS₇PsPiPs) C,P°PjC₇Cr₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇, P° C,P°PePsP₇ PIP»P°C₇PSPëPN₇ PeP»C-C₇P₇PSC₇ P·P°P»PëC₇P°P»PëC₇C₇ PIC-PrPSPsC₇PSPs C₇C,P°P±C-P»CH₇PSPëPjPë. PÿPsPjCr PIP°C₇C-C"PS₇C,P°Pj P· PSPëC₇PePsPIPsC₇ PSP₇PrPsC₇C,P°C,PSC-C₇C,CH₇ PSP₇ PiPsC,C₇C-P±PSP° PePsC₇P₇PeC₇C-C₇ PrPsP·Pë C,P°PjC₇Cr₇P»PsP·PëPSC₇ PiC-PrC₇PsC...P»PsC₇PëPrC₇ PI PeP°PiC₇Cr₇P»P°C.... P₇P»P₇ PIP°C₇C-C"PS₇C,Pë P·

C, P_μ C₇ P_j C - P S P ° P » C H P S P S C H C₁ C, P ° P r C - C " C H P S P e C₇ P e P s P I P s C —
P S P μ P r P s C₁ C, P ° C, P S P s C₁ C, C - (C_{Lcr} < 10 P_j P » / C ... P I / 1, 73 P_j²) P S P μ
P r P s C₁ P » C - P r P ¶ C₁ P I P ° P » P e C₁ C₁.

P_μ P_μ C ‡ C - P S P e P s P I P ° P S P μ P r P s C₁ C, P ° C, P S C - C₁ C, C H

P " C₁ C, P ° C₁ C, P_μ C₇ P e P r

P' P_i P » P e P I P_i P_μ C ‡ C - P S P e P s P I P s C — P S P μ P r P s C₁ C, P ° C, P S P s C₁ C, C - P S P °
C „ P ° C₇ P_j P ° P e P s P e C - P S P μ C, P e P e C_r P r C₁ C, P ° C₁ C, P_μ C₇ P e P r C_r P S P μ P I P e P I C ‡ P ° P I C₁ C₁ (P r P e P I.
C₇ P s P · P r C - P » B « P_μ C₇ P s C, P e P_i P s P e P ° P · P ° P S P S C₁ B »). P h C₁ P e C - P » C H P e P e
P r C_r C, P ° C₁ C, P_μ C₇ P e P r P I P e P I P s P r P e C, C H C₁ C₁ P_i P_μ C₇ P_μ P I P ° P ¶ P S P s C e P » C₁ C ... P s P_j
P_j P_μ C, P ° P ± P s P » C - P · P_j C_r, P s C ‡ C - P e C_r C " C, C H C₁ C₁, C % P s C₇ C - P I P S C -
P r C_r C, P ° C₁ C, P_μ C₇ P e P r C_r P I P_i P » P ° P · P_j C - P e C₇ P s P I C - C ‡ P e C ... P_i P ° C ‡ C - C " P S C, C - P I
P ± C_r P r C_r C, C H P_i C - P r P I P e C % P_μ P S P e P_j P e, P ° P_i P_μ C₇ C - P s P r P S P ° P_i C - P I P I P e P I P_μ P r P_μ P S P S C₁
B H " C, C₇ P e P I P ° P » C - C e P e P_j (P r P e P I. C₇ P s P · P r C - P » P e B « P_Y P_i P s C₁ C - P ±
P · P ° C₁ C, P s C₁ C_r P I P ° P S P S C₁ C, P ° P r P s P · P e B » C - B « P h C₁ P s P ± P » P e P I P s C₁ C, C -
P · P ° C₁ C, P s C₁ C_r P I P ° P S P S C₁ B »).

P_Y P ° P_j C₁ C_r P » P s P · P e P S

P α P ° C₇ P_j P ° P e P s P e C - P S P μ C, P e P e C_r C, P ° P_j C₁ C_r P » P s P · P e P S C_r P_i C - P r C₇ P s C ... P » P s C₇ P e P r C_r
P_i P s C₇ C - P I P S C H P I P ° P » P e C_r 8 P_i P ° C ‡ C - C " P S C, C - P I P · P_i P s P_j C - C₇ P S P e P_j
P_i P s C₇ C_r C e P μ P S P S C₁ P_j C „ C_r P S P e C ‡ C - C — P_i P_μ C ‡ C - P S P e P e (P e P » P ° C₁ P e C „ C - P e P ° C ‡ C - C₁ P · P °
P S P ° P M e P » P r P s P_j B H " P μ B H TM C H: C₁ C, C_r P_i P_μ P S C - A C - B) C - C_r 8 P r P s C₁ P » C - P r P ¶ C₁ P I P ° P S P e C ...
P · P S P s C₇ P_j P ° P » C H P S P S C H C „ C_r P S P e C ‡ C - C " C H P_i P_μ C ‡ C - P S P e P e. P' C, P s P M e C ‡ P ° C₁ C₁ P e
P · P_j C - P S P ° P I P · P ° P_i P ° P » C H P S C - P M e P e P s P S C ‡ P μ P S C, C₇ P ° C ‡ C - C — C, P ° P_j C₁ C_r P » P s P · P e P S C_r
P_i C - P r C₇ P s C ... P » P s C₇ P e P r C_r P I P_i P » P ° P · P_j C - C₁ P_i P s C₁ C, P_μ C₇ C - P_i P ° P » P ° C₁ C₁ P I
C₇ P μ P · C_r P » C H C, P ° C, C - P · P_j C - P S P S P s P_i P s P · P I B H TM C₁ P · C_r P I P ° P S P S C₁ P · P ° P » C H C „ P ° - 1 -
P e P e C₁ P » P e P_j P_i P » C - P e P s P_i C₇ P s C, P μ C — P S P s P_j, P e P s P S C ‡ P μ P S C, C₇ P ° C ‡ C - C₁
P S P μ P · P I B H TM C₁ P · P ° P S P s P_i P s (P ° P e C, P e P I P S P s P_i P s) C, P ° P_j C₁ C_r P » P s P · P e P S C_r
P_i C - P r C₇ P s C ... P » P s C₇ P e P r C_r P S P μ P · P ° P · P S P ° P I P ° P » P ° P · P S P ° C ‡ P S P e C ... P · P_j C - P S,
P I C - P r P · P S P ° C ‡ P ° P » P ° C₁ C₁ C, C - P » C H P e P e P_i P s P_j C - C₇ P S P ° (32 %) P · P_j C - P S P °
P I P » P ° C₁ P S P s P_i P s P e P » C - C₇ P μ P S C₁ C_r P S P μ P · P I B H TM C₁ P · P ° P S P s P_i P s C, P ° P_j C₁ C_r P » P s P · P e P S C_r
P_i C - P r C₇ P s C ... P » P s C₇ P e P r C_r. P_Y P s P_j C_r P_i P ° C ‡ C - C " P S C, P e P · P_i P s P_j C - C₇ P S P e P_j
P_i P s C₇ C_r C e P μ P S P S C₁ P_j C „ C_r P S P e C ‡ C - C — P_i P_μ C ‡ C - P S P e P e P S P μ P_i P s C, C₇ P μ P ± C_r C H C, C H
P e P s C₇ P μ P e C ‡ C - C — P r P s P · P e C, P ° P_j C₁ C_r P » P s P · P e P S C_r P_i C - P r C₇ P s C ... P » P s C₇ P e P r C_r. P " C - C₁
C, P ° P_j C₁ C_r P » P s P · P e P S C_r P_i C - P r C₇ P s C ... P » P s C₇ P e P r C_r P S P μ P I P e P I C ‡ P ° P » P ° C₁ C₁ C_r
P_i P ° C ‡ C - C " P S C, C - P I P · C, C₁ P ¶ P e P e P_j P_i P s C₇ C_r C e P μ P S P S C₁ P_j C „ C_r P S P e C ‡ C - C —
P_i P_μ C ‡ C - P S P e P e.

P' P μ P · P i P μ P e P ° C, P ° P e P » C - P S C - C ‡ P S C - P r P s C₁ P » C - P r P ¶ P μ P S P S C₁.

P_Y P μ C₇ C ‡ P μ P I P ° P S P μ P r P s C₁ C, P ° C, P S C - C₁ C, C H

P_j 4 - C₇ C - C ‡ P S P s P_j C_r P e P » C - P S C - C ‡ P S P s P_j C_r P r P s C₁ P » C - P r P ¶ P μ P S P S C -
P · P ° C₁ C, P s C₁ C_r P I P ° P S P S C₁ P r C_r C, P ° C₁ C, P_μ C₇ P e P r C_r C_r P_i P s C " P r P S P ° P S P S C - P ·
C, P ° P_j C₁ C_r P » P s P · P e P S P s P_j P r P » C₁ P » C - P e C_r P I P ° P S P S C₁ P r P s P ± C₇ P s C₁ P e C - C₁ P S P s C —
P_i C - P_i P μ C₇ P_i P » P ° P · C - C — P_i P μ C₇ P μ P r P_j C - C ... C_r C₇ P s P I P s C — P · P ° P » P s P · P e C_r 4844
C ‡ P s P » P s P I C - P e C - P I (P r P s C₁ P » C - P r P ¶ P μ P S P S C₁ C o m b A T) C ‡ P ° C₁ C, P s C, P °
P I P e P S P e P e P S P μ P S P S C₁ C₁ P μ C₇ C ‡ P μ P I P s C — P S P μ P r P s C₁ C, P ° C, P S P s C₁ C, C - (P · P ± C - C₇ P S P μ
P_i P s P S C₁ C, C, C₁) P I P_i C₇ C_r P_i C - P e P s P_j P ± C - P S P s P I P ° P S P s C — C, P μ C₇ P ° P_i C - C — P ± C_r P » P °

PIPëC%PsCĤ (14/1610, 0,9 %), PSC-P¶ Cr P±CřPrCĤ-CĹPeC-PNë PiCĤCrPïC-
PjPsPSPsC,PµCĤP°PïC-C— PrCřC,P°CĹC,PµCĤPëPrPsPj (4/1623, B B 0,2 %) P°P±Ps
C,P°PjCĹCřP»PsP·PëPSPsPj (10/1611, 0,6 %).

P' PsPeCĤPµPjPsPjCr 4-CĤC-C±PSPsPjCr PeP»C-PSC-C±PSPsPjCr PïPsCĤC-PIPSCLP»CHPSPsPjCr
PrPsCĹP»C-PrP¶PµPSPSC- PïP»P°C†PµP±Ps P· C...C-PjC-C±PSPsCĤ
PïCĤPsC,,C-P»P°PeC,PëPePsCĤ PrCřC,P°CĹC,PµCĤPëPrPsPj P·P° CřC±P°CĹC,CĤ 8231
C±PsP»PsPIC-PeP° PIC-PePsPj PIC-Pr 50 PrPs 75 CĤPsPeC-PI P· PïPsPïPµCĤPµPrPSC-PjPë
PSPµPiP°C,PëPIPSPëPjPë PrP°PSPëPjPë P±C-PsPïCĹC-C— PSP° CĤP°Pe
PïPµCĤPµPrPjC-C...CřCĤPsPIPsC— P·P°P»PsP·Pë C- PIPëC...C-PrPSPëPj CĤC-PIPSPµPj PSA
PjC-P¶ 2,5 PSPI/PjP» C- 10,0 PSPI/PjP» Cř C±PsP»PsPIC-PeC-PI PIC-Pr 50 PrPs 60 CĤPsPeC-PI
P°P±Ps 3 PSPI/PjP» C- 10,0 PSPI/PjP» Cř C±PsP»PsPIC-PeC-PI PIC-PePsPj PïPsPSP°Pr 60
CĤPsPeC-PI (PrPsCĹP»C-PrP¶PµPSPSCĹ REDUCE) P±CřP»Ps PICĹC,P°PSPsPIP»PµPSPs, C%Ps
C±P°CĹC,PsC,P° PIPëPSPëPePSPµPSPSCĹ CĹPµCĤC†PµPIPsC— PSPµPrPsCĹC,P°C,PSPsCĹC,C- Cř
PïP°C†C-C"PSC,C-PI, CĹPeC- PïCĤPëPNëPjP°P»Pë PrCřC,P°CĹC,PµCĤPëPr 0,5 PjPi 1 CĤP°P· PSP°
PrPµPSCĤ (30/4105, 0,7 %), P±CřP»P° PIPëC%PsCĤ PïPsCĤC-PIPSCLPSPs P·
PïP°C†C-C"PSC,P°PjPë, CĹPeC- PïCĤPëPNëPjP°P»Pë PïP»P°C†PµP±Ps B (16/4126, 0,4 %).
P PµC,CĤPsCĹPïPµPeC,PëPIPSPëPNë P°PSP°P»C-P· C†CHPsPiPs PrPsCĹP»C-PrP¶PµPSPSCĹ
PïPsPeP°P·P°PI PIPëC%Cr C±P°CĹC,PsC,Cř CĹPµCĤC†PµPIPsC— PSPµPrPsCĹC,P°C,PSPsCĹC,C-
Cř PïP°C†C-C"PSC,C-PI, CĹPeC- PïCĤPëPNëPjP°P»Pë PrCřC,P°CĹC,PµCĤPëPr C- P°P»CHC,,P°-
P±P»PsPeP°C,PsCĤ PsPrPSPsC±P°CĹPSPs (12/1152, 1,0 %), PïPsCĤC-PIPSCLPSPs P·
CĹCřP±'C"PeC,P°PjPë, CĹPeC- PïCĤPëPNëPjP°P»Pë PrCřC,P°CĹC,PµCĤPëPr P±PµP· P°P»CHC,,P°-
P±P»PsPeP°C,PsCĤP° (18/2953, 0,6 %), PïP»P°C†PµP±Ps C- P°P»CHC,,P°-P±P»PsPeP°C,PsCĤ
(1/1399, <0,1 %) P°P±Ps PïP»P°C†PµP±Ps P±PµP· P°P»CHC,,P°-P±P»PsPeP°C,PsCĤP° (15/2727,
0,6 %). PµCĤPëC±PëPSPSPsPiPs PIP·P°C"PjPsP·PIBĤ™ CĹP·PeCř PjC-P¶
P·P°CĹC,PsCĹCřPIP°PSPSCĹPj PrCřC,P°CĹC,PµCĤPëPrCř (CĹP°PjPsCĹC,C-PNëPSPs P°P±Ps Cř
PePsPjP±C-PSP°C†C-C— P· P°P»CHC,,P°-P±P»PsPeP°C,PsCĤP°PjPë) C,P°
PIPëPSPëPePSPµPSPSCĹPj CĹPµCĤC†PµPIPsC— PSPµPrPsCĹC,P°C,PSPsCĹC,C-
PICĹC,P°PSPsPIP»PµPSPs PSPµ P±CřP»Ps (PrPëPI. CĤPsP·PrC-P» B«PhCĹPsP±P»PëPIPsCĹC,C-
P·P°CĹC,PsCĹCřPIP°PSPSCĹB»).

P P°Pe PïPµCĤPµPrPjC-C...CřCĤPsPIPsC— P·P°P»PsP·Pë C-
PSPëP·CHPePsPrPëC,,PµCĤPµPSC†C-PNëPsPIP°PSC- PïCřC...P»PëPSPë

PJ 4-CĤC-C±PSPsPjCr PrPsCĹP»C-PrP¶PµPSPSC-, PI CĹPePsPjCr PIPëPIC±P°P»Pë PrC-CĤ
PrCřC,P°CĹC,PµCĤPëPrCř PïPsCĤC-PIPSCLPSPs P· PïP»P°C†PµP±Ps, Cř 8231 C±PsP»PsPIC-PeP°
PIC-PePsPj PIC-Pr 50 PrPs 75 CĤPsPeC-PI P· PïPsPïPµCĤPµPrPSC-PjPë PSPµPiP°C,PëPIPSPëPjPë
PrP°PSPëPjPë P±C-PsPïCĹC-C— PSP° CĤP°Pe PïPµCĤPµPrPjC-C...CřCĤPsPIPsC— P·P°P»PsP·Pë
C- PIPëC...C-PrPSPëPj CĤC-PIPSPµPj PSA PjC-P¶ 2,5 PSPI/PjP» C- 10,0 PSPI/PjP» Cř
C±PsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 50 PrPs 60 CĤPsPeC-PI P°P±Ps 3 PSPI/PjP» C- 10,0
PSPI/PjP» Cř C±PsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 60 CĤPsPeC-PI (PrPsCĹP»C-PrP¶PµPSPSCĹ
REDUCE) 6706 CĹCřP±BĤ™C"PeC,P°Pj P±CřP»Ps PïCĤPsPIPµPrPµPSPs PïPsP»PePsPICř
P±C-PsPïCĹC-CĤ PïCĤPsCĹC,P°C,Pë (PsP±PsPIBĤ™ CĹP·PePsPICř P·P° PïPµCĤPIPëPSPSPëPj
PïCĤPsC,PsPePsP»PsPj), PrP°PSC- CĹPePsC— P±CřP»Pë PIPëPePsCĤPëCĹC,P°PSC- PrP»CĹ
P°PSP°P»C-P·Cř PrPëC,,PµCĤPµPSC†C-CĤPIP°PSPSCĹ P·P°B CëPeP°P»PsCĤ P"P»C-CĹPsPSP°. P'
PrPsCĹP»C-PrP¶PµPSPSC- P±CřP»Ps PIPëCĹPIP»PµPSPs 1517 PïP°C†C-C"PSC,C-PI P·
PrC-P°PiPSPsP·PsPj CĤP°Pe PïCĤPsCĹC,P°C,Pë. P'C-P»CHCëC-CĹC,CH PïCřC...P»PëPS
PïCĤPsCĹC,P°C,Pë (70 %), PIPëCĹPIP»PµPSPëC... P·P° PrPsPïPsPjPsPiPsCĤ P±C-PsPïCĹC-C—, PI
PsP±PsC... PïCĤCrPïP°C... P»C-PeCřPIP°PSPSCĹ PjP°P»Pë PIPëCĹPsPePëPNë CĤC-PIPµPSCĤ
PrPëC,,PµCĤPµPSC†C-CĤPIP°PSPSCĹ (5BĤ"6 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P"P»C-CĹPsPSP°).

PJ PïCĤCrPïC- PrCřC,P°CĹC,PµCĤPëPrCř P·P°CĤPµC"CĹC,CĤPsPIP°PSPs P±C-P»CHCë

PIPëCÍPSPeCÍ C±P°CÍC,PsC,CÍ (n = 29, 0,9 %)

PSPëP·CHPePsPrPëC,,PµCĤPµPSC†C-PMëPsPIP°PSPsPiPs CĤP°PeCÍ PiCĤPsCÍC,P°C,Pë (8bĤ“10 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P“P»C-CÍPSPSP°) PiPsCĤC-PIPSCIIPSPs P· PiCĤCÍPiPsCĤ PiP»P°C†PµP±Ps (n = 19, 0,6 %) (CĤ = 0,15). PJ PiPµCĤCëC- 2 CĤPsPePë PrPsCÍP»C-PrP¶PµPSPSCİ PeC-P»CHPeC-CÍC,CH PiP°C†C-C”PSC,C-PI P· CĤP°PePsPj PiPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë P· PiPsPeP°P·PSPëPePsPj 8bĤ“10 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P“P»C-CÍPSPSP° P±CÍP»P° PsPrPSP°PePsPIPsCĤ PI PiCĤCÍPiC- PrCÍC,P°CÍC,PµCĤPëPrCÍ (n 17, 0,5%) C- PI PiCĤCÍPiC- PiP»P°C†PµP±Ps (n = 18, 0,5 %). PµCĤPsC,CİPiPsPj B 3bĤ“4-PiPs CĤPsPeC-PI PrPsCÍP»C-PrP¶PµPSPSCİ P±C-P»CHCëP° PeC-P»CHPeC-CÍC,CH PIPëPiP°PrPeC-PI CĤP°PeCÍ PiPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë P· PiPsPeP°P·PSPëPePsPj 8bĤ“10 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P“P»C-CÍPSPSP° P±CÍP»P° PrC-P°PiPSPsCÍC,PsPIP°PSP° CÍ PiCĤCÍPiC- PrCÍC,P°CÍC,PµCĤPëPrCÍ (n = 12, 0,5 %) PiPsCĤC-PIPSCIIPSPs P· PiCĤCÍPiPsCĤ PiP»P°C†PµP±Ps (n = 1, < 0,1%) (CĤ = 0,0035). PkPµPjP°C” PrP°PSPëC... PiCĤPs PIPiP»PëPI PSP° CĤPëP·PëPe CĤPsP·PIPëC,PeCÍ CĤP°PeCÍ PiCĤPsCÍC,P°C,Pë CÍ C±PsP»PsPIC-PeC-PI, CİPeC- PiCĤPëPNëPjP°CĤC,CH PrCÍC,P°CÍC,PµCĤPëPr PiPsPSP°Pr 4 CĤPsPePë. P’C-PrCÍPsC,PsPe PiP°C†C-C”PSC,C-PI P· PrC-P°PiPSPsP·PsPj CĤP°PeCÍ PiPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë P· PiPsPeP°P·PSPëPePsPj 8bĤ“10 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P“P»C-CÍPSPSP° P·P±PµCĤC-PiP°PICÍCİ PiPsCÍC,C-PMëPSPëPj PI CĤC-P·PSC- PiPµCĤC-PsPrPë PrPsCÍP»C-PrP¶PµPSPSCİ (1bĤ“2-PëPNë CĤPsPePë, 3bĤ“4-PëPNë CĤPsPePë) PI PiCĤCÍPiC- PrCÍC,P°CÍC,PµCĤPëPrCÍ (0,5 % CÍ PePsP¶PSPëPNë PiPµCĤC-PsPr C±P°CÍCÍ), CÍ C,PsPNë C±P°CÍ CİPe CÍ PiCĤCÍPiC- PiP»P°C†PµP±Ps PIC-PrCÍPsC,PsPe PiP°C†C-C”PSC,C-PI C-P· PSPëP·CHPePsPrPëC,,PµCĤPµPSC†C-PMëPsPIP°PSPëPj CĤP°PePsPj PiCĤPsCÍC,P°C,Pë (8bĤ“10 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P“P»C-CÍPSPSP°) P±CÍPI PSPëP¶C±PëPj CÍ 3bĤ“4-C,PëPNë CĤPsPePë, PSC-P¶ PI 1bĤ“2-PëPNë CĤPsPePë (< 0,1 %B C- 0,5 %, PIC-PrPiPsPIC-PrPSPs) (PrPëPI. CĤPsP·PrC-P» B«PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCÍPIP°PSPSCİB»)). PkPµ P±CÍP»Ps PSC-CİPePsC— CĤC-P·PSPëC†C- PI C±P°CÍC,PsC,C- PIPëPiP°PrPeC-PI CĤP°PeCÍ PiPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë P· PiPsPeP°P·PSPëPePsPj 7bĤ“10 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P“P»C-CÍPSPSP° (CĤ = 0,81).

PJ 4-CĤC-C±PSPsPjCÍ PeP»C-PSC-C±PSPsPjCÍ PrPsCÍP»C-PrP¶PµPSPSC- P»C-PeCÍPIP°PSPSCİ PrPsP±CĤPsCİPeC-CÍPSPsC— PiC-PiPµCĤPiP»P°P·C-C— PiPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·PëB (CombAT), PrPµB PiPµCĤPIPëPSPSPëPj PiCĤPsC,PsPePsP»PsPj PSPµ P±CÍP»Ps PiPµCĤPµPrP±P°C±PµPSPs PsP±PsPiBĤ™ CİP·PePsPICÍ P±C-PsPiCÍC-CĤ C- PICÍC- PrC-P°PiPSPsP·Pë CĤP°PeCÍ PiCĤPsCÍC,P°C,Pë P±CÍP»Pë PICÍC,P°PSPsPIP»PµPSC- PSP° P±C-PsPiCÍC-C— P·P° PiPsPeP°P·P°PSPSCİPjPë, C±P°CÍC,PsC,P° PIPëPiP°PrPeC-PI CĤP°PeCÍ PiPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë P· PiPsPeP°P·PSPëPePsPj 8bĤ“10 P±P°P»C-PI P·P° CëPeP°P»PsCĤ P“P»C-CÍPSPSP° P±CÍP»P° 0,5 % (n = 8) CÍ PiCĤCÍPiC- PrCÍC,P°CÍC,PµCĤPëPrCÍ 0,7 % (n=11), CÍ PiCĤCÍPiC- C,P°PjCÍCÍP»PsP·PëPSCÍ C,P° 0,3% (n=5) CÍ PiCĤCÍPiC- PePsPjP±C-PSPsPIP°PSPsC— C,PµCĤP°PiC-C—.

P—PiBĤ™ CİP·PsPe PjC-P¶ P·P°CÍC,PsCÍCÍPIP°PSPSCİPj PrCÍC,P°CÍC,PµCĤPëPrCÍ C,P° PIPëPSPëPePSPµPSPSCİPj PSPëP·CHPePsPrPëC,,PµCĤPµPSC†C-PMëPsPIP°PSPsPiPs CĤP°PeCÍ PiPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë P·P°P»PëCëP°C”C,CHCÍCİ PSPµP·BĤ™ CİCÍPsPIP°PSPëPj.

P P°Pe PiCĤCÍPrPSPsC— P·P°P»PsP·Pë Cé C±PsP»PsPIC-PeC-PI

P”PIP° PIPëPiP°PrPsPe-PePsPSC,CĤPsP»CHPsPIP°PSC- PµPiC-PrPµPjC-PsP»PsPiC-C±PSC- PrPsCÍP»C-PrP¶PµPSPSCİ, PsPrPSPµ PiCĤPsPIPµPrPµPSPs CÍ PŸPëPĥ B B B B B B B B B B B B B B B B (n=339 PIPëPiP°PrPeC-PI CĤP°PeCÍ PiCĤCÍPrPSPsC— P·P°P»PsP·Pë C- n=6780 CÍ PiCĤCÍPiC- PePsPSC,CĤPsP»CĤ), P° C-PSCëPµ CÍ P’PµP»PëPeC-PNë

$P'CHPeC, P^{\circ}PSC-C$ — B B B B B B ($n = 398$ $PIP\ddot{e}P^{\circ}PrPeC-PI$ $CHP^{\circ}PeCr$ $PiCHCrPrPSPsC-$
 $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e} C-$ $n=3930$ Cr $PiCHCrPiC-$ $PePsPSC, CHPsP \gg CH$) Cr $P \pm P^{\circ}P\cdot P^{\circ}C \dots PrP^{\circ}PSP\ddot{e}C \dots$
 $PsC \dots PsCHPsPSP\ddot{e} P\cdot PrPsCHPsPI\ddot{e}H^{\text{TM}} C\ddot{I}$, PSP_{μ} $PiPsPeP^{\circ}P\cdot P^{\circ}P \gg P\ddot{e} PSC-C\ddot{I}PePsPiPs$
 $P\cdot P \pm C-P \gg CHC\epsilon P_{\mu}PSPSC\ddot{I}$ $CHP\ddot{e}P\cdot P\ddot{e}PeCr$ $CHPsP\cdot PIP\ddot{e}C, PeCr$ $CHP^{\circ}PeCr$ $PiCHCrPrPSPsC-$
 $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e} Cr$ $C \ddagger PsP \gg PsPIC-PeC-PI$ $PiCHP\ddot{e} P\cdot P^{\circ}C\ddot{I}C, PsC\ddot{I}CrPIP^{\circ}PSPSC-$
 $C-PSiC-P \pm C-C, PsCHC-PI$ $5\alpha-CHP_{\mu}PrCrPeC, P^{\circ}P\cdot P\ddot{e}$. P $P_{\mu}P\cdot CrP \gg CHC, P^{\circ}C, P\ddot{e}$ $PiP_{\mu}CHC\epsilon PsPiPs$
 $PrPsC\ddot{I}P \gg C-PrP\parallel P_{\mu}PSPSC\ddot{I}$ PSP_{μ} $PIP\ddot{e}C\ddot{I}PIP\ddot{e}P \gg P\ddot{e}$ $PiPsP\cdot P\ddot{e}C, P\ddot{e}PIPSPsPiPs$
 $PIP\cdot P^{\circ}C''PjPsP\cdot PI\ddot{e}H^{\text{TM}} C\ddot{I}P\cdot PeCr$ $P\cdot$ $CHP^{\circ}PePsPj$ $PiCHCrPrPSPsC-$ $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e}$
 $(PIC-PrPSPsC\ddot{I}PSP\ddot{e}PN_{\ddot{e}}$ $CHP\ddot{e}P\cdot P\ddot{e}Pe$ $PrP \gg C\ddot{I}$ 3 1 $CHPsPeCr$ $P\cdot P^{\circ}C\ddot{I}C, PsC\ddot{I}CrPIP^{\circ}PSPSC\ddot{I}$ $PrPs$
 $PIC\ddot{I}C, P^{\circ}PSPsPIP \gg P_{\mu}PSPSC\ddot{I}$ $PrC-P^{\circ}PiPSPsP\cdot Cr$ $CHP^{\circ}PeCr$ $PiCHCrPrPSPsC-$ $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e}$
 $PiPsCHC-PIPSC\ddot{I}PSPs$ $P\cdot < 1$ $CHPsPeCr$ $P\cdot P^{\circ}C\ddot{I}C, PsC\ddot{I}CrPIP^{\circ}PSPSC\ddot{I}$: $0,70: 95 \%$ $P''P \ddagger 0,34, 1,45$).
 Pj $PrCHCrPiPsPjCr$ $PrPsC\ddot{I}P \gg C-PrP\parallel P_{\mu}PSPSC-$ $PsC \ddagger C-PSp_{\mu}PSP\ddot{e}PN_{\ddot{e}}$ $PIC-PrPSPsC\ddot{I}PSP\ddot{e}PN_{\ddot{e}}$
 $CHP\ddot{e}P\cdot P\ddot{e}Pe$ $CHP^{\circ}PeCr$ $PiCHCrPrPSPsC-$ $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e}$, $PiPsPI\ddot{e}H^{\text{TM}} C\ddot{I}P\cdot P^{\circ}PSP\ddot{e}PN_{\ddot{e}}$ $C-P\cdot$
 $P\cdot P^{\circ}C\ddot{I}C, PsC\ddot{I}CrPIP^{\circ}PSPSC\ddot{I}Pj$ $C-PSiC-P \pm C-C, PsCHC-PI$ $5\alpha-CHP_{\mu}PrCrPeC, P^{\circ}P\cdot P\ddot{e}$
 $PiPsCHC-PIPSC\ddot{I}PSPs$ $P\cdot C, P^{\circ}PeP\ddot{e}Pj$ $PiCHP\ddot{e}$ $PIC-PrC\ddot{I}CrC, PSPsC\ddot{I}C, C-$
 $P\cdot P^{\circ}C\ddot{I}C, PsC\ddot{I}CrPIP^{\circ}PSPSC\ddot{I}$ $C\ddot{I}C, P^{\circ}PSPsPIP\ddot{e}PI$ $1,08: 95 \%$ $P''P \ddagger 0,62, 1,87$).

$P_{\mu}CHPeC \ddagger P\ddot{e}PSPSP\ddot{e}PN_{\ddot{e}}$ $PIP\cdot P^{\circ}C''PjPsP\cdot PI\ddot{e}H^{\text{TM}} C\ddot{I}P\cdot PsPe$ $PjC-P\parallel$ $PIP\ddot{e}P^{\circ}PrPeP^{\circ}PjP\ddot{e}$ $CHP^{\circ}PeCr$
 $PiCHCrPrPSPsC-$ $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e} Cr$ $C \ddagger PsP \gg PsPIC-PeC-PI$ C, P° $PrPsPIPiPsC, CHP\ddot{e}PIP^{\circ}P \gg P\ddot{e}Pj$
 $P\cdot P^{\circ}C\ddot{I}C, PsC\ddot{I}CrPIP^{\circ}PSPSC\ddot{I}Pj$ $PrCrC, P^{\circ}C\ddot{I}C, P_{\mu}CHP\ddot{e}PrCr$ PSP_{μ} $PIC\ddot{I}C, P^{\circ}PSPsPIP \gg P_{\mu}PSPs$.

$P_{\mu}P \gg C-PSC-C \ddagger PSC- C \dots P^{\circ}CHP^{\circ}PeC, P_{\mu}CHPeC\ddot{I}C, P\ddot{e}PeP\ddot{e}$.

$P_{\mu}PsPeP^{\circ}P\cdot P^{\circ}PSPSC\ddot{I}$.

$P \gg C-PeCrPIP^{\circ}PSPSC\ddot{I}$ $PiPsPjC-CHPSP\ddot{e}C \dots C, P^{\circ} C, C\ddot{I}P\parallel PeP\ddot{e}C \dots C\ddot{I}P\ddot{e}PjPiC, PsPjC-PIB$
 $PrPsP \pm CHPsC\ddot{I}PeC-C\ddot{I}PSPsC-$ $PiC-PiP_{\mu}CHPiP \gg P^{\circ}P\cdot C-C-$ $PiP_{\mu}CHP_{\mu}PrPjC-C \dots CrCHPsPIPsC-$
 $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e}$.

$P-PjP_{\mu}PSC\epsilon P_{\mu}PSPSC\ddot{I}$ $CHP\ddot{e}P\cdot P\ddot{e}PeCr$ $PIP\ddot{e}PSP\ddot{e}PePSP_{\mu}PSPSC\ddot{I}$ $PiPsC\ddot{I}C, CHPsC-$
 $P\cdot P^{\circ}C, CHP\ddot{e}PjPeP\ddot{e}$ $C\ddot{I}P_{\mu}C \ddagger C-$ C, P° $PSP_{\mu}PsP \pm C \dots C-PrPSPsC\ddot{I}C, C-$ $C \dots C-CHCrCHPiC-C \ddagger PSPsPiPs$
 $PIC, CHCrC \ddagger P^{\circ}PSPSC\ddot{I}$ Cr $PiP^{\circ}C \ddagger C-C''PSC, C-PI$ $P\cdot$ $PiPsPjC-CHPSP\ddot{e}PjP\ddot{e}$ $C, P^{\circ} C, C\ddot{I}P\parallel PeP\ddot{e}PjP\ddot{e}$
 $C\ddot{I}P\ddot{e}PjPiC, PsPjP^{\circ}PjP\ddot{e}$ $PrPsP \pm CHPsC\ddot{I}PeC-C\ddot{I}PSPsC-$ $PiC-PiP_{\mu}CHPiP \gg P^{\circ}P\cdot C-C-$
 $PiP_{\mu}CHP_{\mu}PrPjC-C \dots CrCHPsPIPsC-$ $P\cdot P^{\circ}P \gg PsP\cdot P\ddot{e}$.

$P_{\mu}CHPsC, P\ddot{e}PiPsPeP^{\circ}P\cdot P^{\circ}PSPSC\ddot{I}$.

$P''CrPsPrP^{\circ}CHC, PSP_{\mu}$ $P\cdot P^{\circ}C\ddot{I}C, PsC\ddot{I}PsPICrCHC, CH$ $PrP \gg C\ddot{I}$ $P \gg C-PeCrPIP^{\circ}PSPSC\ddot{I}$
 $P\parallel C-PSPsPe C-$ $PrC-C, P_{\mu}PN_{\ddot{e}}$ ($PrP\ddot{e}PI$. $CHPsP\cdot PrC-P \gg B \ll P-P^{\circ}C\ddot{I}C, PsC\ddot{I}CrPIP^{\circ}PSPSC\ddot{I}$ Cr
 $PiP_{\mu}CHC-PsPr$ $PIP^{\circ}PiC-C, PSPsC\ddot{I}C, C-$ $P^{\circ}P \pm Ps$ $PiPsPrCrPIP^{\circ}PSPSC\ddot{I}$ $PiCHCrPrPrCHB \gg$).

$P''CrPsPrP^{\circ}CHC, PiCHPsC, P\ddot{e}PiPsPeP^{\circ}P\cdot P^{\circ}PSP\ddot{e}PN_{\ddot{e}}$ $C \dots PIPsCHP\ddot{e}Pj$ $P\cdot$
 $PiC-PrPIP\ddot{e}C \%$ $P_{\mu}PSPsCHB$ $C \ddagger CrC, P \gg P\ddot{e}PIC-C\ddot{I}C, CH$ $PrPs$ $PrCrC, P^{\circ}C\ddot{I}C, P_{\mu}CHP\ddot{e}PrCr,$
 $C-PSC\epsilon P\ddot{e}C \dots C-PSiC-P \pm C-C, PsCHC-PI$ $5\alpha-CHP_{\mu}PrCrPeC, P^{\circ}P\cdot P\ddot{e}$, $C, P^{\circ}PjC\ddot{I}CrP \gg PsP\cdot P\ddot{e}PSCr$
 $(PIPeP \gg CHC \ddagger P^{\circ}CHC \ddagger P\ddot{e}$ $C, P^{\circ}PjC\ddot{I}CrP \gg PsP\cdot P\ddot{e}PSC-PSPrCrPePsPIP^{\circ}PSP\ddot{e}PN_{\ddot{e}}$
 $P^{\circ}PSiC-PsPSP_{\mu}PICCHPsC, P\ddot{e}C \ddagger PSP\ddot{e}PN_{\ddot{e}}$ $PSP^{\circ}P \pm CHC\ddot{I}Pe$), $C-PSC\epsilon P\ddot{e}C \dots PePsPjPiPsPSP_{\mu}PSC, C-PI$
 $PiCHP_{\mu}PiP^{\circ}CHP^{\circ}C, Cr$ $P^{\circ}P \pm Ps$ $PrPs$ $C\ddot{I}PsC-$ $C-$ $P^{\circ}CHP^{\circ}C \dots C-C\ddot{I}Cr$.

$\text{P}\mu\text{C}\overline{\text{H}}\text{P}\overline{\text{e}}\text{ PrPsPIPiPsC}\overline{\text{f}}\text{C}, \text{C}\overline{\text{H}}\text{PsPePsPIPsPjC}\overline{\text{r}}\text{ P}\cdot\text{P}^{\circ}\text{C}\overline{\text{f}}\text{C}, \text{PsC}\overline{\text{f}}\text{C}\overline{\text{r}}\text{PIP}^{\circ}\text{PSPSC}-\text{PePsPjP}\pm\text{C}-\text{PSP}^{\circ}\text{C}\overline{\text{f}}\text{C}-\text{C}-$
 $\text{PrC}\overline{\text{r}}\text{C}, \text{P}^{\circ}\text{C}\overline{\text{f}}\text{C}, \text{P}\mu\text{C}\overline{\text{H}}\text{P}\overline{\text{e}}\text{PrC}\overline{\text{r}}\text{ P}\cdot\text{P}\gg\text{C}-\text{PeP}^{\circ}\text{C}\overline{\text{H}}\text{C}\overline{\text{f}}\text{CHbPeP}\overline{\text{e}}\text{PjP}\overline{\text{e}}\text{ P}\cdot\text{P}^{\circ}\text{C}\overline{\text{f}}\text{PsP}\pm\text{P}^{\circ}\text{PjP}\overline{\text{e}}, \text{C}\overline{\text{f}}\text{PeC}-\text{C}''$
 $\text{C}\overline{\text{f}}\text{P}\overline{\text{e}}\text{P}\gg\text{CHbPSPsPrC}-\text{CHC}\ddagger\text{P}\overline{\text{e}}\text{PjP}\overline{\text{e}}\text{ C}-\text{PSPiC}-\text{P}\pm\text{C}-\text{C}, \text{PsC}\overline{\text{H}}\text{P}^{\circ}\text{PjP}\overline{\text{e}}\text{ C}, \text{P}\mu\text{C}\overline{\text{H}}\text{PjP}\mu\text{PSC}, \text{C}\overline{\text{r}}\text{ CYP3A4}$
 $(\text{PSP}^{\circ}\text{PiC}\overline{\text{H}}\text{P}\overline{\text{e}}\text{PeP}\gg\text{P}^{\circ}\text{Pr}: \text{C}\overline{\text{H}}\text{P}\overline{\text{e}}\text{C}, \text{PsPSP}^{\circ}\text{PIC}-\text{C}\overline{\text{H}}, \text{C}-\text{PSPrP}\overline{\text{e}}\text{PSP}^{\circ}\text{PIC}-\text{C}\overline{\text{H}}, \text{PSP}\mu\text{C}, \text{P}^{\circ}\text{P}\cdot\text{PsPrPsPS},$
 $\text{C}-\text{C}, \text{C}\overline{\text{H}}\text{P}^{\circ}\text{PePsPSP}^{\circ}\text{P}\cdot\text{PsP}\gg, \text{PeP}\mu\text{C}, \text{PsPePsPSP}^{\circ}\text{P}\cdot\text{PsP}\gg, \text{C}\overline{\text{f}}\text{PeC}-\text{PIIPsPrP}\overline{\text{e}}\text{P}\gg\text{P}\overline{\text{e}}$
 $\text{PiP}\mu\text{C}\overline{\text{H}}\text{PsC}\overline{\text{H}}\text{P}^{\circ}\text{P}\gg\text{CHbPSPs}), \text{PePsPSC}\overline{\text{f}}\text{P}\mu\text{PSC}, \text{C}\overline{\text{H}}\text{P}^{\circ}\text{C}\overline{\text{f}}\text{C}-\text{C}\overline{\text{f}}\text{ PrC}\overline{\text{r}}\text{C}, \text{P}^{\circ}\text{C}\overline{\text{f}}\text{C}, \text{P}\mu\text{C}\overline{\text{H}}\text{P}\overline{\text{e}}\text{PrC}\overline{\text{r}}\text{ PI}$

PhPrPSPSc†P°C†PSPμ P·P°C†C,PsC†C†PIP°PSPSC‡ C,P°PjC†C†P»PsP·PëPSCr
PiC-PrC‡PsC...P»PsC‡PëPrCr C,P° PePμC,PsPePsPSP°P·PsP»Cr (C†PëP»C‡PSPsPiPs
C-PSPiC-P±C-C,PsC‡P° CYP3A4)B B P·P±C-P»C‡C€C†C" PŸ_{max} C,P° AUC
C,P°PjC†C†P»PsP·PëPSCr PiC-PrC‡PsC...P»PsC‡PëPrCr Cr 2,2 C,P° 2,8 C‡P°P·P°

PIC-PrPⁱPsPIC-PrPSPs.

P^YC^rPjC-C^rPSP_μ P·P°C^rC,PsC^rC^rPIP°PSPSC_μ C,P°PjC^rC^rP»PsP·PēPSC^r
PiC-PrC_μPsC...P»PsC_μPēPrC^r C,P° PⁱP°C_μPsPeC^rP_μC,PēPSC^r (C^rPēP»CH_μPSPsPiPs
C-PSPiC-P±C-C,PsC_μP° CYP2D6) P·P±C-P»CH_μCēC^rC^r P^Y_{max} C,P° AUC C,P°PjC^rC^rP»PsP·PēPSC^r
PiC-PrC_μPsC...P»PsC_μPēPrC^r C^r 1,3 C,P° 1,6 C_μP°P·P° PIC-PrPⁱPsPIC-PrPSPs.
P_μPSP°P»PsPiC-C_μPSP_μ P·P±C-P»CH_μCēP_μPSPSC_μ PsC_μC-PeC^rC^rC,CH_μC^rC_μ C^r
PⁱP°C^rC-C^rPSC,C-PI P·C- C^rP»P°P±PePēPj PjP_μC,P°P±PsP»C-P·PjPsPj CYP2D6
PⁱPsC_μC-PIPSC_μPSPs P· C,P°PePēPjPē P· C-PSC,P_μPSC^rPēPIPSPēPj PjP_μC,P°P±PsP»C-P·PjPsPj
PⁱC_μPē C^rC^rPjC-C^rPSPsPjC^r P·P°C^rC,PsC^rC^rPIP°PSPSC- P· C^rPēP»CH_μPSPēPjPē
C-PSPiC-P±C-C,PsC_μP°PjPē CYP3A4.

P·C,,P_μPeC, C^rC^rPjC-C^rPSPsPiPs P·P°C^rC,PsC^rC^rPIP°PSPSC_μ PsP±PsC...
C-PSPiC-P±C-C,PsC_μC-PI CYP3A4 C,P° C-PSPiC-P±C-C,PsC_μC-PI CYP2D6 P·
C,P°PjC^rC^rP»PsP·PēPSPsPj PeP»C-PSC-C_μPSPs PSP_μ PrPsC^rP»C-PrP^μC^rPIP°PIC^rC_μ, PsPrPSP°Pe
PⁱPsC,P_μPSC^rC-PM_μPSPs PjPsP^μP_μ C^rC^rC,C,C^rPIPs P·P±C-P»CH_μCēC^rPIP°C,PēC^rC_μ
PePsPSC^rP_μPSC,C_μP°C^rC-C_μ C,P°PjC^rC^rP»PsP·PēPSC^r (PrPēPI. C_μPsP·PrC-P»
B«PhC^rPsP±P»PēPIPsC^rC,C- P·P°C^rC,PsC^rC^rPIP°PSPSC_μB»).

PhPrPSPsC_μP°C^rPSP_μ P·P°C^rC,PsC^rC^rPIP°PSPSC_μ C,P°PjC^rC^rP»PsP·PēPSC^r
PiC-PrC_μPsC...P»PsC_μPēPrC^r (0,4 PjPi) C- C_μPēPjP_μC,PēPrPēPSC^r (400 PjPi PePsP^μPSC- 6
PiPsPrPēPS PⁱC_μPsC,C_μPiPsPj 6 PrPSC-PI) PⁱC_μPēP·PIPsPrPēP»Ps PrPs P·PSPēP^μP_μPSPSC_μ
PeP»C-C_μP_μPSC^rC^r (26 %) C- P·P±C-P»CH_μCēP_μPSPSC_μ AUC (PⁱP»PsC%_μC- PⁱC-Pr
C,,P°C_μPjP°PePsPeC-PSP_μC,PēC_μPSPsC_μ PeC_μPēPIPsC_μ) (44 %) C,P°PjC^rC^rP»PsP·PēPSC^r
PiC-PrC_μPsC...P»PsC_μPēPrC^r. P^rC^rPsPrP°C_μC, C^rP»C-Pr P· PsP±P_μC_μP^μP^μPSC-C^rC,C_μ
P·P°C^rC,PsC^rPsPIC^rPIP°C,Pē PI PePsPjP±C-PSP°C^rC-C— P· C_μPēPjP_μC,PēPrPēPSPsPj.

P^rPēC_μP_μC_μPⁱPSP_μ PrPsC^rP»C-PrP^μP_μPSPSC_μ PIP·P°C^rPjPsPrC-C— C,P°PjC^rC^rP»PsP·PēPSC^r
PiC-PrC_μPsC...P»PsC_μPēPrC^r C- PIP°C_μC,,P°C_μPēPSC^r PSP_μ PⁱC_μPsPIPsPrPēP»PsC^rC_μ.
P P_μP·C^rP»CH_μC,P°C,Pē PsP±PjP_μP^μP_μPSPēC... PrPsC^rP»C-PrP^μP_μPSC_μ *in vitro* C,P° *in vivo* C^r
PSP_μPrPsC^rC,P°C,PSC-PjPē. P— PsP±P_μC_μP_μP^μPSC-C^rC,C_μ C^rP»C-Pr PⁱC_μPsPIPsPrPēC,Pē
PsPrPSPsC_μP°C^rPSP_μ P»C-PeC^rPIP°PSPSC_μ PIP°C_μC,,P°C_μPēPSPsPj C-
C,P°PjC^rC^rP»PsP·PēPSC^r PiC-PrC_μPsC...P»PsC_μPēPrPsPj.

P^kC-C_μPePsC— PIP·P°C^rPjPsPrC-C— PSP_μ C^rPⁱPsC^rC,P_μC_μC-PiP°P»PsC^rC_μ, PePsP»Pē
C,P°PjC^rC^rP»PsP·PēPSC^r PiC-PrC_μPsC...P»PsC_μPēPr PⁱPIPsPrPēP»Pē PsPrPSPsC_μP°C^rPSPs P·
P°C,P_μPSPsP»PsP»PsPj P°P±Ps P_μPSP°P»PⁱC_μPēP»PsPj, P°P±Ps PSC-C,,P_μPrPēPiC-PSPsPj,
P°P±Ps C,P_μPsC,,C-P»C-PSPsPj. PhPrPSPsC_μP°C^rPSP_μ P·P°C^rC,PsC^rC^rPIP°PSPSC_μ
C,,C^rC_μPsC^rP_μPjC-PrC^r PⁱC_μPēP·PIPsPrPēC,CH PrPs P·PSPēP^μP_μPSPSC_μ C_μC-PIPSC-PI
C,P°PjC^rC^rP»PsP·PēPSC^r PI C^rPēC_μPsPIP°C,C^rC- PeC_μPsPIC-, P°P»P_μ, PsC^rPeC-P»CH_μPePē
C^rC- C_μC-PIPSC- P·P°P»PēCēP°C_μC,CH_μC^rC_μ C^r PjP_μP^μP°C... PSPsC_μPjP°P»CH_μPSPsPiPs
PrC-P°PⁱP°P·PsPSC^r, PePsC_μP_μPeC^rC-C_μ PrPsP·Pē PSP_μ PⁱPsC,C_μC-P±PSP°.

P^r C^rPjPsPIP°C... *in vitro* PSC- PrC-P°P·P_μPⁱP°Pj, PSC- PⁱC_μPsPⁱC_μP°PSPsP»PsP», PSC-
C,C_μPēC...P»PsC_μPjP_μC,C-P°P·PēPr, PSC- C...P»PsC_μPjP°PrPēPSPsPS, PSC-
P°PjC-C,C_μPēPiC,PēP»C-PS, PSC- PrPēPeP»PsC,,P_μPSP°Pe, PSC- PiP»C-P±P_μPSPeP»P°PjC-Pr,
PSC- C^rPēPjPIP°C^rC,P°C,PēPS PSP_μ P·PjC-PSC_μC_μC,CH PIC-P»CH_μPSC^r C,,C_μP°PeC^rC-C_μ
C,P°PjC^rC^rP»PsP·PēPSC^r C^r PⁱP»P°P·PjC- PeC_μPsPIC- P»CH_μPrPēPSPē. P^YP°PjC^rC^rP»PsP·PēPS
C,P°PePsP^μ PSP_μ P·PjC-PSC_μC^r PIC-P»CH_μPSC- C,,C_μP°PeC^rC-C— PrC-P°P·P_μPⁱP°PjC^r,
PⁱC_μPsPⁱC_μP°PSPsP»PsP»C^r, C,C_μPēC...P»PsC_μPjP_μC,C-P°P·PēPrC^r C-
C...P»PsC_μPjP°PrPēPSPsPSC^r.

***$P\hbar C\acute{I}P_sP\pm P\gg P\ddot{e}PIP_sC\acute{I}C,C-$
 $P\cdot P^{\circ}C\acute{I}C,P_sC\acute{I}C\acute{e}PIP^{\circ}PSPSC\Pi.$***

PuPsP±C-C±PSC- CḡPuP°PeC†C-C— P· P±PsPeCṛ CḡPuCḡC†PuPIPs-CḡCṛPrPëPSPSPsC—
CḡPëCḡC,PuPjPë

$\text{P}\mu\text{C}\overline{\text{H}}\text{PsPIP}\mu\text{PrP}\mu\text{PSPs}$ $\text{PjP}\mu\text{C}, \text{P}^\circ\text{P}^\circ\text{PSP}^\circ\text{P} \gg \text{C-P} \cdot 12$ $\text{C}\overline{\text{H}}\text{P}^\circ\text{PSPrPsPjC-P} \cdot \text{PsPIP}^\circ\text{PSP}\ddot{\text{C}}\dots$,
 $\text{PiP} \gg \text{P}^\circ\text{C}\ddagger\text{P}\mu\text{P} \pm \text{Ps-}$ $\text{P}^\circ\text{P} \pm \text{Ps}$ $\text{PiPsC}\overline{\text{H}}\text{C-PIPSC}\overline{\text{H}} \gg \text{C}\overline{\text{H}}\text{PSP}\ddot{\text{C}}\dots$ $\text{PePsPSC}, \text{C}\overline{\text{H}}\text{PsP} \gg \text{C}\overline{\text{H}}\text{PsPIP}^\circ\text{PSP}\ddot{\text{C}}\dots$
 $\text{PeP} \gg \text{C-PSC-C} \pm \text{PSP}\ddot{\text{C}}\dots$ $\text{PrPsC}\overline{\text{H}}\text{P} \gg \text{C-PrP}\overline{\text{H}}\text{P}\mu\text{PSC}\overline{\text{H}}$ ($n=18802$), PI $\text{C}\overline{\text{H}}\text{PePsPjC}\overline{\text{r}}$

PsC†C-PSC†PIP°P»Pë C†PëP·PëPe C†PsP·PIPëC,PeC† P†PsP±C-C†PSPëC... C†PµP°PeC†C-PNë P·
P±PsPeC† C†PµC†PµPIP±C†C†PrPëPSPSPsC— C†PëC†C,PµPjPë P†C†Pë
P·P°C†C,PsC†C†PIP°PSPSC- PrC†C,P°C†C,PµC†PëPrC† (P†PsC†C-PIPSC†PSPs P·
PePsPSC,C†PsP»C†PSPsC† P†C†C†P†PsC†). P†Pµ P±C†P»Ps PIC†C,P°PSPsPIP»PµPSPs
C†C,C-PNëPePsPiPs C†C,P°C,PëC†C,PëC†PSPs P·PSP°C†C†C%oPsPiPs P·P±C-P»C†C†PµPSPSC†
C†PëP·PëPeC†B C†PµC†PµPIP±C— PSPµPrPsC†C,P°C,PSPsC†C,C- (RR 1,05; 95 % P†P† 0,71,
1,57), P†PsC†C,C†PsPiPs C-PSC,P°C†PeC,C† PjC-PsPeP°C†PrP° B B B B B B B B B B (RR 1,00;
95 % P†P† 0,77, 1,30) P°P±Ps C-PSC†C†P»C†C,C† (RR 1,20; 95 % P†P† 0,88, 1,64).

P P°Pe P†PµC†PµPrPjC-C...C†C†PsPIP±C— P·P°P»PsP·Pë C,P° P†C†C...P»PëPSPë PIPëC†PsPePsPiPs
C†C,C†P†PµPSC† P†C†P°PrP°C†C-C— P·P° P†P»C-C†PsPSPsPj (PSPëP·C†PePs-
PrPëC,,PµC†PµPSC†C-PNëPsPIP°PSC-)

Pj C...PsPrC- 4-C†C-C†PSPsPiPs PeP»C-PSC-C†PSPsPiPs PrPsC†P»C-PrP¶PµPSPSC† P·P°
C†C†P°C†C,C† > 8000 C†PsP»PsPIC-PeC-PI PIC-PePsPj PIC-Pr 50 PrPs 75 C†PsPeC-PI P·
P†PsPiPµC†PµPrPSC†PsC† PSPµPiP°C,PëPIPSPsC† P±C-PsPiC†C-C†C† PSP° C†P°Pe
P†PµC†PµPrPjC-C...C†C†PsPIP±C— P·P°P»PsP·Pë C,P° C,,PsPSPsPIPëPj C†C-PIPSPµPj PSA PjC-P¶
2,5 PSp†PjP» C,P° 10,0 PSp†PjP» (PrPsC†P»C-PrP¶PµPSPSC† REDUCE) C† 1517
C†PsP»PsPIC-PeC-PI P±C†P»Ps PrC-P°PiPSPsC†C,PsPIP°PSPs C†P°Pe
P†PµC†PµPrPjC-C...C†C†PsPIP±C— P·P°P»PsP·Pë. P†C-PrP·PSP°C†P°P»P°C†C† PIPëC%oP°
C†P°C†C,PsC,P° PIPëPSPëPePSPµPSPSC† C†P°PeC† P†PµC†PµPrPjC-C...C†C†PsPIP±C—
P·P°P»PsP·Pë P· PrPëC,,PµC†PµPSC†C-C†PIP°PSPSC†Pj 8B†“10 P±P°P»C-PI P·P° C†PeP°P»PsC†
P†P»C-C†PsPSP° C† P†C†C†P†C- PrC†C,P°C†C,PµC†PëPrC† (n=29, 0,9 %) P†PsC†C-PIPSC†PSPs
P· P†C†C†P†PsC† P†P»P°C†PµP±Ps (n=19, 0,6 %). PµC†PëC†PëPSPSPsPiPs
PIP·P°C†PjPsP·P†B†™ C†P·PeC† PjC-P¶ P·P°C†C,PsC†C†PIP°PSPSC†Pj PrC†C,P°C†C,PµC†PëPrC†
C,P° PIPëPSPëPePSPµPSPSC†Pj PSPëP·C†PePsPrPëC,,PµC†PµPSC†C-PNëPsPIP°PSPsPiPs
C†P°PeC† P†PµC†PµPrPjC-C...C†C†PsPIP±C— P·P°P»PsP·Pë PIC†C,P°PSPsPIP»PµPSPs PSPµ
P±C†P»Ps. P†P»C-PSC-C†PSP° P·PSP°C†C†C%oC-C†C,C† C†PëC,,C†PsPIP±Ps
PrPëC†P±P°P»P°PSC†C† PSPµ PIC†C,P°PSPsPIP»PµPSP°.B

P§PsP»PsPIC-PePë, C†PeC- P·P°C†C,PsC†PsPIC†C†C,C† P†C†PsPrP°C†C,, PjP°C†C,C†
C†PµPiC†P»C†C†PSPs P†C†PsC...PsPrPëC,Pë PsP±C†C,PµP¶PµPSPSC† C%oPsPrPs
PIPëP·PSP°C†PµPSPSC† C†PëP·PëPeC† C†PsP·PIPëC,PeC† C†P°PeC†
P†PµC†PµPrPjC-C...C†C†PsPIP±C— P·P°P»PsP·Pë, PIPëP»C†C†P°C†C†Pë C,PµC†C, PSP°
P†C†PsC†C,P°C,-C†P†PµC†PëC,,C-C†PSPëPNë P°PSC,PëPiPµPS.

Pj PrPsPrP°C,PePsPiPsPjC† P†PsC†P»C-PrPsPIPSPsPjC† 2-C†C-C†PSPsPjC†
C†P†PsC†C,PµC†PµP¶PµPSPSC- PsC†PëPiC-PSP°P»C†PSPëC... P†P°C†C-C†PSC,C-PI P†C†Pë
P·P°C†C,PsC†C†PIP°PSPSC- B PrC†C,P°C†C,PµC†PëPrC† PI C†PePsC†C,C- C...C-PjC-C†PSPsC—
P†C†PsC,,C-P»P°PeC,PëPePë (PrPsC†P»C-PrP¶PµPSPSC† REDUCE) P±C†P»P°
PIC†C,P°PSPsPIP»PµPSP° PSPëP·C†PeP° C†P°C†C,PsC,P° PSPsPIPëC... PIPëP†P°PrPeC-PI
C†P°PeC† P†PµC†PµPrPjC-C...C†C†PsPIP±C— P·P°P»PsP·Pë (P†C†C†P†P°
PrC†C,P°C†C,PµC†PëPrC† [n=14, 1,2 %]) C,P° P†C†C†P†P° P†P»P°C†PµP±Ps [n=7, 0,7 %]) P·
PIC-PrC†C†C,PSC-C†C,C† PSPsPIPëC... C-PrPµPSC,PëC,,C-PePsPIP°PSPëC... PIPëP†P°PrPeC-PI
C†P°PeC† P†PµC†PµPrPjC-C...C†C†PsPIP±C— P·P°P»PsP·Pë P·
PrPëC,,PµC†PµPSC†C-C†PIP°PSPSC†Pj 8B†“10 P±P°P»C-PI P·P° C†PeP°P»PsC†
P†P»C-C†PsPSP°.

P†PµPiPsC,C†PëPIP°P»Pµ P†PsC†P»C-PrPsPIPSPµ (PrPs 18 C†PsPeC-PI)
C†P†PsC†C,PµC†PµP¶PµPSPSC† P†P°C†C-C†PSC,C-PI P· PeP»C-PSC-C†PSPsPiPs
PrPsC†P»C-PrP¶PµPSPSC† C-P· P·P°C†C,PsC†C†PIP°PSPSC†Pj C-PSC†PsPiPs
C-PSPiC-P±C-C,PsC†P° 5α-C†PµPrC†PeC,P°P·Pë (C,,C-PSP°C†C,PµC†PëPrC†) PI C†PePsC†C,C-

C...C-PjC-C†PSPsC— P†CḡPsC,,C-P»P°PeC,PëPePë PSPµ P†PsPeP°P·P°P»Ps
C†C,P°C,PëC†C,PëC†PSPs P·PSP°C†CrC%PsC— CḡC-P·PSPëC†C- PjC-P¶ P†CḡCrP†P°PjPë
C,,C-PSP°C†C,PµCḡPëPrCr C,P° P†P»P°C†PµP±Ps Cr P†PsPeP°P·PSPëPeP°C...
P·P°P†P°P»CHPSPsP†Ps P†PëP¶PëP†P°PSPSC† (HR1,02, 95 % P”P† 0,97Бḡ“1,08) P°P±Ps
P†PëP¶PëP†P°PSPSC† P†C-C†P»C† P†C-P°P†PSPsC†C,C†P†P°PSPSC† CḡP°PeCr
P†PµCḡPµPrPjC-C...CrCḡPsP†PsC— P·P°P»PsP·Pë (HR1,01, 95 % P”P† 0,85Бḡ“1,20).B B B

P†P†P»PëP† PSP° P†CḡPsC†C,P°C,-C†P†PµC†PëC,,C-C†PSPëPNë P°PSC,PëP†PµPS (PSA)

PḡPsPSC†PµPSC,CḡP°C†C-C† P†CḡPsC†C,P°C,-C†P†PµC†PëC,,C-C†PSPsP†Ps P°PSC,PëP†PµPSC†
P†PµCḡPµPrPjC-C...CrCḡPsP†PsC— P·P°P»PsP·Pë (PSA) B C” P†P°P¶P»PëP†PëPj
PePsPjP†PsPSPµPSC,PsPj C†PeCḡPëPSC-PSP†PsP†PsP†Ps P†CḡPsC†PµC†C† P†P»C†
P†PëC†P†P»PµPSPSC† CḡP°PeCr P†PµCḡPµPrPjC-C...CrCḡPsP†PsC— P·P°P»PsP·Pë.
P”CrC,P°C†C,PµCḡPëPr P·PrP°C,PSPëPNë P·PSPëP¶C†P†P°C,Pë CḡC-PIPµPSCḡ
C†PëCḡPsP†P°C,PePsP†PsP†Ps P†CḡPsC†C,P°C,-C†P†PµC†PëC,,C-C†PSPsP†Ps P°PSC,PëP†PµPSC† Cr
C...P†PsCḡPëC... P†CḡPëP±P»PëP·PSPs PSP° 50 % C†PµCḡPµP· 6 PjC-C†C†C†C-PI
P»C-PëC†P†P°PSPSC†.

PµP°C†C-C”PSC,Pë, C†PeC- P†CḡPëPNëPjP°CḡC,CH P”CrPsPrP°CḡC,, P†PsP†PëPSPSC- PjP°C,Pë
PSPsP†PëPNë P†PëC...C-PrPSPëPNë CḡC-PIPµPSCḡ PSA, P†C†C,P°PSPsP†P»PµPSPëPNë C†PµCḡPµP·
6 PjC-C†C†C†C-PI P†C-C†P»C† P»C-PëC†P†P°PSPSC† C†PëPj P†CḡPµP†P°CḡP°C,PsPj.
PḡP°PrP°P»C- C†PµPNë CḡC-PIPµPSCḡ CḡPµPePsPjPµPSP†CrC”C,CHC†C†
P†PµCḡPµPIC-CḡC†C,Pë CḡPµP†CrP»C†CḡPSPs. P”CrPrCH-C†PePµ P†C-PrC,PIPµCḡPrP¶PµPSPµ
P·P±C-P»CHC€PµPSPSC† CḡC-PIPSC† PSA PIC-Pr PSP°PNëPSPëP¶C†PsP†Ps CḡC-PIPSC† P†C-Pr
C†P°C† P·P°C†C,PsC†C†P†P°PSPSC† P”CrPsPrP°CḡC,C† PjPsP¶Pµ P±CrC,Pë
C†PIC-PrC†PµPSPSC†Pj PSP°C†P†PSPsC†C,C- CḡP°PeCr P†PµCḡPµPrPjC-C...CrCḡPsP†PsC—
P·P°P»PsP·Pë P°P±Ps PSPµPrPsC,CḡPëPjP°PSPSC† CḡPµP¶PëPjCr P»C-PëC†P†P°PSPSC†
P”CrPsPrP°CḡC,PsPj C- P†PsC,CḡPµP±CrC” CḡPµC,PµP»CHPSPsP†Ps P†PëPIC†PµPSPSC†,
PSP°PIC-C,CH C†PeC%Ps P†PsPeP°P·PSPëPePë PSA P·PSP°C...PsPrC†C,CHC†C† C†
PjPµP¶P°C... PSPsCḡPjPë Cr C†PsP»PsPIC-PëC-PI, C†PeC- PSPµ P»C-PëC†P†P°P»PëC†CH
C-PSP†C-P±C-C,PsCḡP°PjPë 5α-CḡPµPrCrPeC,P°P·Pë. PµCḡPë C-PSC,PµCḡP†CḡPµC,P°C†C-C—
P†PsPeP°P·PSPëPeC-PI PSA Cr C...P†PsCḡPëC..., C†PeC- P»C-PëC†CḡC,CHC†C†
P”CrPsPrP°CḡC,PsPj, C†P»C-Pr P·P†P°P¶P°C,Pë PSP° P†PsP†PµCḡPµPrPSC- P†PsPeP°P·PSPëPePë
PSA PrP»C† P†PsCḡC-PIPSC†PSPSC†.

P—P°C†C,PsC†C†P†P°PSPSC† P”CrPsPrP°CḡC,C† PSPµ P†P†P»PëP†P°C” PSP°
P†PëPePsCḡPëC†C,P°PSPSC† CḡC-PIPSC† P†CḡPsC†C,P°C,-C†P†PµC†PëC,,C-C†PSPsP†Ps
P°PSC,PëP†PµPSC† PrP»C† P†C-P°P†PSPsC†C,PëPePë CḡP°PeCr
P†PµCḡPµPrPjC-C...CrCḡPsP†PsC— P·P°P»PsP·Pë P†C-C†P»C† PIC†C,P°PSPsP†P»PµPSPSC†
PNëPsP†Ps PSPsP†PsP†Ps P†PëC...C-PrPSPsP†Ps CḡC-PIPSC†.

P—P°P†P°P»CHPSPëPNë CḡC-PIPµPSCḡ C†PëCḡPsP†P°C,PePsP†PsP†Ps P†CḡPsC†C,P°C,-
C†P†PµC†PëC,,C-C†PSPsP†Ps P°PSC,PëP†PµPSC† P†PsP†PµCḡC,P°C”C,CHC†C† P†Ps
P†PëC...C-PrPSPsP†Ps CḡC-PIPSC† P†CḡPsC,C†P†PsPj 6 PjC-C†C†C†C-PI P†C-C†P»C†
P†CḡPëP†PëPSPµPSPSC† P»C-PëC†P†P°PSPSC†.

PŸP†C-PIPIC-PrPSPsC€PµPSPSC† P¶ PIC-P»CHPSPsP†Ps P†CḡPsC†C,P°C,-
C†P†PµC†PëC,,C-C†PSPsP†Ps P°PSC,PëP†PµPSC† C- P·P°P†P°P»CHPSPsP†Ps PNëPsP†Ps
CḡC-PIPSC† P·P°P»PëC€P°C”C,CHC†C† C†C,P°P»PëPj PSP°PIC-C,CH P†C-Pr C†P°C†
P»C-PëC†P†P°PSPSC† P”CrPsPrP°CḡC,PsPj. P†PeC%Ps PrP»C† P†PëP·PSP°C†PµPSPSC†
CḡP°PeCr P†PµCḡPµPrPjC-C...CrCḡPsP†PsC— P·P°P»PsP·Pë P»C-PëP°Cḡ P†PëCḡC-C€PëC,CH
P†PëPePsCḡPëC†C,P°C,Pë PIC-PrC†PsC,PePsP†PëPNë P†PsPeP°P·PSPëPe PIC-P»CHPSPsP†Ps

ΠΐCΉPsCΓC, P°C, -CΓΐΠΐC†PēC,, C-C†PSPsPiPs P°PSC, PēPiPμPSCr CΓ C... PIPsCΉPsPiPs, CΐPePēPN₂
P»C-PeCΓC"C, CHCΓCΐ P"CΓPsPrP°CΉC, PsPj, PSC-CΐPePsPiPs PePsCΉPμPiCΓPIP°PSPSCΐ
ΠΐPsPeP°P·PSPēPeP° PIC-P»CHPSPsPiPs ΠΐCΉPsCΓC, P°C, -CΓΐΠΐC†PēC,, C-C†PSPsPiPs
P°PSC, PēPiPμPSCr ΠΐCΉPsPiPsPrPēC, Pē PSPμ ΠΐPsC, CΉC-P±PSPs.

PμPμCΉPμPr ΠΐPsC†P°C, PePsPj PeCΓCΉCΓCΓ P»C-PeCΓPIP°PSPSCΐ P"CΓPsPrP°CΉC, PsPj C, P°
ΠΐPμCΉC-PsPrPēC†PSPs ΠΐC-Pr C†P°CΓ P»C-PeCΓPIP°PSPSCΐ ΠΐP°C†C-C"PSC, P°Pj P·
PrPsP±CΉPsCΐPeC-CΓPSPsCΉ ΠΐC-ΠΐPμCΉΠΐP»P°P·C-C"CΉ ΠΐPμCΉPμPrPjC-C... CΓCΉPsPiPsC—
P·P°P»PsP·Pē CΓP»C-Pr CΉPsP±PēC, Pē ΠΐP°P»CHC†PμPIPμ CΉPμPeC, P°P»CHPSPμ
PsP±CΓC, PμP¶PμPSPSCΐ, P° C, P°PePsP¶ P·P°CΓC, PsCΓPsPICΓPIP°C, Pē C-PSC€C- PjPμC, PsPrPē
PIPēCΐPIP»PμPSPSCΐ CΉP°PeCΓ ΠΐPμCΉPμPrPjC-C... CΓCΉPsPiPsC— P·P°P»PsP·Pē.

PκPēCΉPePsPIP° PSPμPrPsCΓC, P°C, PSC-CΓC, CH

P>C-PeCΓPIP°PSPSCΐ C... PIPsCΉPēC... P· C, CΐP¶PePsCΉ PSPēCΉPePsPiPsCΉ
PSPμPrPsCΓC, P°C, PSC-CΓC, CΉB (PeP»C-CΉPμPSCΓ PeCΉPμP°C, PēPSC-PSCr < 10 PjP»/C...PI)
ΠΐPsC, CΉC-P±PSPs ΠΐCΉPsPiPsPrPēC, Pē P· PsP±PμCΉPμP¶PSC-CΓC, CΉ, PsCΓPeC-P»CHPePē
C,, P°CΉPjP°PePsPeC-PSPμC, PēPeP° PrCΓC, P°CΓC, PμCΉPēPrCΓ CΓ C, P°PePēC... C... PIPsCΉPēC...
PSPμ PIPēPIC†P°P»P°CΓCΉ.

PϋCΉC, PμCΉC-P°P»CHPSP° ΠΐC-ΠΐPsC, PμPSP·C-Cΐ

PμPsPrC-P±PSPs PrPs C-PSC€PēC... P°P»CHC,, P°1-P°PrCΉPμPSPsP±P»PsPeP°C, PsCΉC-PI,
PsCΉC, PsCΓC, P°C, PēC†PSP° ΠΐC-ΠΐPsC, PμPSP·C-Cΐ PjPsP¶Pμ PIPēPSPēPePSCrC, Pē CΓ
ΠΐP°C†C-C"PSC, C-PI, CΐPeC- P»C-PeCΓPIP°P»PēCΓCΐ C, P°PjCΓCΓP»PsP·PēPSPsPj, C- CΓ
CΉC-PrPeC-CΓPSPēC... PIPēΠΐP°PrPeP°C... PjPsP¶Pμ ΠΐCΉPēP·PIPμCΓC, Pē PrPs CΓPēPSPePsPiPμ.

PμCΉPē ΠΐPμCΉC€PēC... PsP·PSP°PeP°C... PsCΉC, PsCΓC, P°C, PēC†PSPsC— ΠΐC-ΠΐPsC, PμPSP·C-C—
(P·P°ΠΐP°PjPsCΉPsC†PμPSPSCΐ, CΓP»P°P±PeC-CΓC, CΉ) ΠΐP°C†C-C"PSC, C-PI, CΐPeC-
CΉPsP·ΠΐPsC†P°P»Pē P»C-PeCΓPIP°PSPSCΐ P"CΓPsPrP°CΉC, PsPj, CΓP»C-Pr ΠΐPμCΉPμPIPμCΓC, Pē
CΓ ΠΐPsP»PsP¶PμPSPSCΐ CΓPēPrCΐC†Pē P°P±Ps P»PμP¶P°C†Pē, ΠΐPsPePē CΓPēPjΠΐC, PsPjPē PSPμ
PjPēPSCrC, CΉ.

PŸP»C-Pr PrPsC, CΉPēPjCΓPIP°C, PēCΓCΉ PsP±PμCΉPμP¶PSPsCΓC, C- ΠΐCΉPē
CΓCΓPjC-CΓPSPsPjCΓ P·P°CΓC, PsCΓCΓPIP°PSPSC- P°P»CHC,, P°-
P°PrCΉPμPSPsP±P»PsPeP°C, PsCΉC-PI, PIPeP»CΉC†P°CΉC†Pē C, P°PjCΓCΓP»PsP·PēPS, C, P°
C-PSPiC-P±C-C, PsCΉC-PI 5-C,, PsCΓC,, PsPrC-PμCΓC, PμCΉP°P·Pē. PϋP»CHC,, P°-
P°PrCΉPμPSPsP±P»PsPeP°C, PsCΉPē C, P° C-PSPiC-P±C-C, PsCΉPē 5-
C,, PsCΓC,, PsPrC-PμCΓC, PμCΉP°P·Pē C" PIP°P·PsPrPēP»P°C, P°C, PsCΉP°PjPē C, P° PjPsP¶CΓC, CH
P·PSPēP¶CΓPIP°C, Pē P°CΉC, PμCΉC-P°P»CHPSPēPN₂ C, PēCΓPe. PŸCΓPjC-CΓPSPμ
P·P°CΓC, PsCΓCΓPIP°PSPSCΐ C†PēC... PrPIPSC... PeP»P°CΓC-PI P»C-PeP°CΉCΓCΉPePēC...
P·P°CΓPsP±C-PI PjPsP¶Pμ ΠΐPsC, PμPSC†C-PN₂PSPs CΓΠΐCΉPēC†PēPSPēC, Pē
CΓPēPjΠΐC, PsPjP°C, PēC†PSCr P°CΉC, PμCΉC-P°P»CHPSCr ΠΐC-ΠΐPsC, PμPSP·C-CΉ (PrPēPI.
CΉPsP·PrC-P» B<P·P·P°C"PjPsPrC-Cΐ P· C-PSC€PēPjPē P»C-PeP°CΉCΓCΉPePēPjPē
P·P°CΓPsP±P°PjPē C, P° C-PSC€C- PIPēPrPē PIP·P°C"PjPsPrC-PN₂B»).

P†PSC, CΉP°PsPiPμCΉP°C†C-PN₂PSPēPN₂ CΓPēPSPrCΉPsPj P°C, PsPSC-C†PSPsC—
CΉP°PN₂PrCΓP¶PePē

PμC-Pr C†P°CΓ PsΠΐPμCΉP°C†C-C— P· ΠΐCΉPēPiPsPrCΓ PeP°C, P°CΉP°PeC, Pē C, P°
ΠΐP»P°CΓPePsPjPē CΓ PrPμCΐPePēC... ΠΐP°C†C-C"PSC, C-PI, CΐPeC- CΉP°PSC-C€Pμ
PsC, CΉPēPjCΓPIP°P»Pē C, P°PjCΓCΓP»PsP·PēPS, P±CΓPI PIC-PrP·PSP°C†PμPSPēPN₂

C-PSC, C₇H₆P°PsP_iP_μC₇H₆P°C†C-PM₂PSP₂P₂ C₇H₆PSP₂PrC₇H₆PsP_j P°C, PsPSC-C₇PSP₂Sc—
C₇H₆P°PM₂PrC₇PrP₂PeP₂ (P†P₂P₂ , PIP°C₇H₆-P°PSC, C₇H₆PSP₂PrC₇H₆PsP_jCr PIC₇Pr·CH₆PePsC—
P·C-PSP₂C†C-). P†PSC, C₇H₆P°PsP_iP_μC₇H₆P°C†C-PM₂PSP₂P₂ C₇H₆PSP₂PrC₇H₆PsP_j P°C, PsPSC-C₇PSP₂Sc—
C₇H₆P°PM₂PrC₇PrP₂PeP₂ P_jPsP₂PrP₂ P_iC₇H₆P₂·PIP_μC₇H₆, P₂ PrPs P·P±C-P»CH₆C₇PrP₂PSPSC₇
C₇H₆P₂·P₂PeC₇ PsC₇PSP₂C... CrC₇PrP₂»P°PrPSP_μPSC₇ P_iC-Pr C₇P°C₇ P°P±Ps P_iC-C₇Pr»C₇
PsP_iP_μC₇H₆P°C†C-C—. P₂PsP_jCr P»C-PeC₇PIP°PSPSC₇ P°C₇PsPrP°C₇H₆, PsP_j PSP_μ
C₇H₆PePsP_jP_μPSP₂PrC₇C, CH₆C₇C₇ P_iP°C†C-C°PSC, P°P_j, C₇PrP₂ P·P°P_i»P°PSP₂PIP°PSP₂
PsP_iP_μC₇H₆P°C†C-C₇ P· P_iC₇H₆PIP₂PrC₇ PeP°C, P°C₇H₆PeC, P₂.

P_μC-Pr C₇P°C₇ P_iP_μC₇H₆PrPsP_iP_μC₇H₆P°C†C-PM₂PSP₂P_iPs PsP±C₇H₆, P_μP₂PrP₂PSPSC₇
C...C-C₇H₆C₇PrP_i-PsC,, C, P°P»CH₆P_jPsP»PsP_i C- PM₂PsP_iPs P±C₇H₆P_iP°PrP° P_jP°C₇H₆, CH₆
P·B₇™ C₇C₇C₇PrP_iP°C, P₂, C₇P₂ P_iC₇H₆P₂·PSP°C₇P°P»P₂ P_iP°C†C-C°PSC, PsPIC- C₇H₆P°PSC-C₇PrP₂
P°P±Ps C, P_μP_iP_μC₇ P°C₇PsPrP°C₇H₆,. P_iP_μ PrP°C₇H₆, CH₆ P·P_jPsP_iCr P_iP_μC₇H₆PrP±P°C₇P₂, P₂
P_jPsP₂»P₂P_iCr P_iPsC₇PrP_iCr C-PSC, C₇H₆P°PsP_iP_μC₇H₆P°C†C-PM₂PSP₂P_iPs C₇H₆PSP₂PrC₇H₆PsP_jCr
P°C, PsPSC-C₇PSP₂Sc— C₇H₆P°PM₂PrC₇PrP₂PeP₂ P_iC-Pr C₇P°C₇ PsP_iP_μC₇H₆P°C†C-C—.

P_hC, C₇H₆P₂P_jP°PSP₂ P_iPsPsPrP₂PSP₂PeC- P_iPsPIC-PrPsP_jP»P_μPSPSC₇ P_iC₇H₆Ps
P_iPsP·P₂C, P₂PIPSP₂P₂ P_μC,, P_μPeC, PIC-PrP_jC-PSP₂ C, P°P_jC₇CrP»PsP·P₂PSC₇ P·P° 1B₇“2
C, P₂P₂PSC- PrPs PsP_iP_μC₇H₆P°C†C-C— P· P_iC₇H₆PIP₂PrC₇ PeP°C, P°C₇H₆PeC, P₂ C, P°
P_iP»P°C₇PePsP_jP₂, PsPrPSP°Pe P_iP_μC₇H₆PIP°P_iP₂ C, P° C₇H₆PsPeP₂ P_iC₇H₆P₂P₂PSP_μPSPSC₇
P»C-PeC₇PIP°PSPSC₇ PrPs PsP_iP_μC₇H₆P°C†C-C— P· P_iC₇H₆PIP₂PrC₇ PeP°C, P°C₇H₆PeC, P₂ C, P°
P_iP»P°C₇PePsP_jP₂ PSP_μ PIC₇H₆, P°PSP₂PIP»P_μPSC-.

P_hP_μP_iP_μC₇H₆P_jP_μC, P₂C₇PSC- PeP°P_iC₇CrP»P₂

P°C₇H₆, P°C₇H₆, P_μC₇H₆Pr P°P±C₇PsC₇H₆P±C₇C, CH₆C₇C₇ C₇P_μC₇H₆Pr· C₇PeC-C₇Cr, C, PsP_jCr
P₂C-PSP₂PeP₂ C, P° PrC-C, P₂ P_jP°C₇H₆, CH₆ CrPSP₂PeP°C, P₂ PePsPSC, P°PeC, Cr P·
PSP_μP_iP_μC₇H₆P_jP_μC, P₂C₇PSP₂P_jP₂ PeP°P_iC₇CrP»P°P_jP₂. P_iPeC%Ps C₇H₆-PrP₂PSP° P·
PeP°P_iC₇CrP»P₂ P_iPsC, C₇H₆P_iP₂»P° PSP° C₇PeC-C₇Cr, C—C— C₇Pr»C-Pr PSP_μP_iP°PM₂PSP₂
P·P_jP₂C, P₂ PIP₂PrPsC₇ P· P_jP₂»PsP_j.

P†PSP_iC-P±C-C, PsC₇H₆P₂ P₂YP3A4 C, P° CYP2D6

P₂CrP_jC-C₇PSP_μ P·P°C₇H₆, PsC₇CrP_iP°PSPSC₇ C, P°P_jC₇CrP»PsP·P₂PSC₇
P_iC-PrC₇PsC...P»PsC₇H₆PrC₇ P· C₇H₆P»CH₆PSP₂P_jP₂ C-PSP_iC-P±C-C, PsC₇H₆P_jP₂ P₂YP3A4
(PSP°P_iC₇H₆PeP»P°Pr PeP_μC, PsPePsPSP°P·PsP»PsP_j) P°P±Ps B₇“ Cr P_jP_μPSC₇C-PM₂ P_jC-C₇H₆-
B₇“ P· C₇H₆P»CH₆PSP₂P_jP₂ C-PSP_iC-P±C-C, PsC₇H₆P_jP₂ CYP2D6 (PSP°P_iC₇H₆PeP»P°Pr
P_iP°C₇H₆PsPeC₇P_μC, P₂PSP₂P_j) P_jPsP₂PrP₂ P·P±C-P»CH₆C₇CrP_iP°C, P₂ PePsPSC†P_μPSC, C₇H₆P°C†C-C₇
C, P°P_jC₇CrP»PsP·P₂PSC₇ (PrP₂PI. C₇H₆PsP·PrC-P» B«P·P·P°C”P_jPsPrC-C₇ P· C-PSC₇PeP_jP₂
P»C-PeP°C₇C₇CH₆PeP_jP₂ P·P°C₇PsP±P°P_jP₂ C, P° C-PSC₇C- PIP₂PrP₂ PIP·P°C”P_jPsPrC-PM₂B»).
P₂PsP_jCr PSP_μ C₇H₆PePsP_jP_μPSP₂PrC₇C, CH₆C₇C₇ P·P°C₇H₆, PsC₇PsPIC₇PrP°C, P₂
C, P°P_jC₇CrP»PsP·P₂PS P_iP°C†C-C°PSC, P°P_j, C₇PrP₂ P»C-PeC₇C₇, CH₆C₇C₇
C₇H₆P»CH₆PSP₂P_jP₂ C-PSP_iC-P±C-C, PsC₇H₆P_jP₂ P₂YP3A4, C, P° C₇H₆PePsP_jP_μPSP₂PrPsPIP°PSP₂
P· PsP±P_μC₇H₆P₂P₂PSC-C₇H₆ P·P°C₇H₆, PsC₇PsPIC₇PrP°C, P₂ C, P°P_jC₇CrP»PsP·P₂PS
P_iP°C†C-C°PSC, P°P_j, C₇PrP₂ P»C-PeC₇C₇, CH₆C₇C₇ P_iPsP_jC-C₇H₆PSP₂P_jP₂
C-PSP_iC-P±C-C, PsC₇H₆P_jP₂ P₂YP3A4 (PSP°P_iC₇H₆PeP»P°Pr P_μC₇H₆C, C₇H₆PsP_jC-C†P₂PSP₂P_j),
C₇H₆P»CH₆PSP₂P_jP₂ P°P±Ps P_iPsP_jC-C₇H₆PSP₂P_jP₂ C-PSP_iC-P±C-C, PsC₇H₆P_jP₂ CYP2D6,
PePsP_jP±C-PSP°C†C-C°C₇ PsP±PsC... P₂YP3A4 C, P° CYP2D6 C-PSP_iC-P±C-C, PsC₇H₆-PI P°P±Ps
P_iP°C†C-C°PSC, P°P_j P·C- C₇Pr»P°P±PeP_j P_jP_μC, P°P±PsP»C-P·P_jPsP_j CYP2D6.

P_μP_μC₇C-PSP₂PePsPIP° PSP_μPrPsC₇H₆, P°C, PSC-C₇H₆, CH₆

P'P'P»PëPI P'PµC‡C-PSPePsPIPsC— PSPµPrPsC'fC,P°C,PSPsC'fC,C- PSP°
C,,P°C'fCp'p°PePsPeC-PSPµC,PëPeC'fB PrC'fC,P°C'fC,PµC'fPëPrC'f PSPµ PIPëPIC‡P°PIC'fC'fC.
P'PµC'fPµP· P°PeC,PëPIPSpëPNë PjPµC,P°P±PsP»C-P·Pj PrC'fC,P°C'fC,PµC'fPëPrC'f C,P° 3B'f"5-
C,Pë C,PëP'fPSPµPIPëPNë P'PµC'fC-PsPr PNëPsPiPs PSP°P'fC-PIPIPëPIPµPrPµPSPSC'fC
P»C-PeC'fPIP°PSPSC'fC PrC'fC,P°C'fC,PµC'fPëPrPsPj C...PIPsC'fPëC... P· P»PµPiPePsC'f P°P±Ps
P'PsPjC-C'fPSPsC'f P'PµC‡C-PSPePsPIPsC'f PSPµPrPsC'fC,P°C,PSC-C'fC,C'f C'fP»C-Pr
P'fC'fPsPIPsPrPëC,Pë P· PsP±PµC'fPµP'fPSC-C'fC,C'f (PrPëPI. C'fPsP·PrC-P»Pë B«P'fPiPsC'fC-P±
P·P°C'fC,PsC'fC'fPIP°PSPSC'fC C,P° PrPsP·PëB», B«PµC'fPsC,PëP'fPsPeP°P·P°PSPSC'fC»B»,
B«PαP°C'fPjP°PePsP»PsPiC-C‡PSC- PIP»P°C'fC,PëPIPsC'fC,C-B»).

P"PsPiPsPjC-P'fPSC- C'fPµC‡PsPIPëPSPë

P"CrPsPrP°C'fC, PjC-C'fC,PëC,C'f P±P°C'fPIPSPëPe FD&C Yellow 6 (E 110), C%oPs PjPsP'fPµ
C'fPiC'fPëC‡PëPSPëC,Pë P°P»PµC'fPiC-C‡PSC- C'fPµP°PeC‡C-C—.

P P°Pe PiC'fC'fPrPSPsC— P·P°P»PsP·Pë Cr C‡PsP»PsPIC-PeC-PI

PµPsPIC-PrPsPjP»C'fP»PsC'fC'f P'fC'fPs C'fC-PrPeC-C'fPSC- PIPëPiP°PrPePë C'fP°PeC'f
PiC'fC'fPrPSPsC— P·P°P»PsP·Pë Cr C‡PsP»PsPIC-PeC-PI P'fC-Pr C‡P°C'f PeP»C-PSC-C‡PSPëC...
PrPsC'fP»C-PrP'fPµPSC'f C,P° Cr PiPsC'fC,PjP°C'fPePµC,PëPSPiPsPIPëPNë P'PµC'fC-PsPr. PµC'fPë
C‡C'fPsPjC'f PµP'fC-PrPµPjC-PsP»PsPiC-C‡PSC- PrPsC'fP»C-PrP'fPµPSPSC'fC PIPeP°P·C'fC'fC,C'f
PSP° PIC-PrC'fC'fC,PSC-C'fC,C'f P'fC-PrPIPëC%oPµPSPSC'fC C'fPëP·PëPeC'f C'fPsP·PIPëC,PeC'f
C'fP°PeC'f PiC'fC'fPrPSPsC— P·P°P»PsP·Pë Cr C‡PsP»PsPIC-PeC-PI P'fC'fPë
P·P°C'fC,PsC'fC'fPIP°PSPSC- C-PSPiC-P±C-C,PSC'fC-PI 5α-C'fPµPrC'fPeC,P°P·Pë. P»C-PeP°C'fC-
PiPsPIPëPSPSC- PiPsPiPµC'fPµPrPëC,Pë C'fPIPsC—C... PiP°C‡C-C"PSC,C-PI P'fC'fPs
PSPµPsP±C...C-PrPSC-C'fC,C'f PSPµPiP°PNëPSPs PiPsPIC-PrPsPjP»C'fC,Pë P'fC'fPs P±C'fPrC'f-
C'fPeC- P·PjC-PSPë Cr C,PeP°PSPëPSC- PiC'fC'fPrPSPsC— P·P°P»PsP·Pë, PSP°P'fC'fPëPeP»P°Pr
P'fC'fPs PIPëPrC-P»PµPSPSC'fC C-P· C'fPsC'fPeP° P°P±Ps P'fC'fPëP'fC'fC...P»C-C'fC,C'f.

***P—P°C'fC,PsC'fC'fPIP°PSPSC'fC C'f P'PµC'fC-PsPr PIP°PiC-C,PSPsC'fC,C- P°P±Ps
PiPsPrC'fPIP°PSPSC'fC PiC'fC'fPrPrC'f.***

P"CrPsPrP°C'fC, P'fC'fPsC,PëP'fPsPeP°P·P°PSPëPNë PrP»C'f P»C-PeC'fPIP°PSPSC'fC P'fC-PSPsPe.
P"PsC'fP»C-PrP'fPµPSPSC'fC P· PIPëPIC‡PµPSPSC'fC PIPiP»PëPIC'f P"CrPsPrP°C'fC,C'f PSP°
PIP°PiC-C,PSC-C'fC,C'f, P»P°PeC,P°C‡C-C'f C,P° C,,PµC'fC,PëP»C'fPSC-C'fC,C'f PSPµ
P'fC'fPsPIPsPrPëP»Pë. P"°P»C- PSP°PrP°C"C,C'fC'fC'f C-PSC,PSC'fPjP°C‡C-C'f P'fC'fPs
P·P°C'fC,PsC'fC'fPIP°PSPSC'fC PePsP'fPSPsPiPs PePsPjPiPsPSPµPSC,P° PsPeC'fPµPjPs.

PαPµC'fC,PëP»C'fPSC-C'fC,C'f.

P"CrC,P°C'fC,PµC'fPëPr PIPiP»PëPIP°C" PSP° C...P°C'fP°PeC,PµC'fPëC'fC,PëPePë
PµC'fPeC'fP»C'fC,C'f (P·PjPµPSC€PµPSPSC'fC PeC-P»C'fPePsC'fC,C-
C'fPiPµC'fPjP°C,PsP·PsC—PrC-PI, PsP±B'f™C" PjC'f PµC'fPeC'fP»C'fC,C'f C,P°
C'fC'fC...PsPjPsC'fC,C- C'fPiPµC'fPjP°C,PsP·PsC—PrC-PI). P'fPµ PIPëPeP»C'fC‡PµPSPëPNë
C'fPëP·PëPe P·PSPëP'fPµPSPSC'fC C‡PsP»PsPIC-C‡PsC— C,,PµC'fC,PëP»C'fPSPsC'fC,C-.

P'fC‡C-PSPeP° PIPiP»PëPIC'f C,P°PjC'fC'fP»PsP·PëPSC'f PiC-PrC'fPsC...P»PsC'fPëPrC'f PSP°
PeC-P»C'fPeC-C'fC,C'f P°P±Ps C,,C'fPSPeC‡C-C'f C'fPiPµC'fPjP°C,PsP·PsC—PrC-PI PSPµ
P'fC'fPsPIPsPrPëP»P°C'fC'fC.

P°P°PiC-C,PSC-CÍC,CH.

PİPe C- C-PSC€C- C-PSPiC-P±C-C,PsCȚPë 5α-CȚPμPrCřPeC,P°P·Pë, PrCřC,P°CÍC,PμCȚPëPr
PiPμCȚPμC€PePsPrP¶P°C” PiPμCȚPμC,PIPsCȚPμPSPSCȚ C,PμCÍC,PsCÍC,PμCȚPsPSCř Cř
PrPëPiC-PrCȚPsC,PμCÍC,PsCÍC,PμCȚPsPS, C°Ps PjPsP¶Pμ PiP°P»CHPjCřPIP°C,Pë
CȚPsP·PIPëC,PsPe P·PsPIPSC-C€PSC-C... CÍC,P°C,PμPIPëC... PsCȚPiP°PSC-PI Cř PiP»PsPrP°
C±PsP»PsPIC-C±PsC— CÍC,P°C,C-. PkPμP·PSP°C±PSCř PeC-P»CHPeC-CÍC,CH
PrCřC,P°CÍC,PμCȚPëPrCř P±CřP»Ps PIPëCȚPIIP»PμPSPs PI PμCȚPeCřP»CȚC,C- PiCȚPë
PiCȚPsPIPμPrPμPSPSC- PrPsCÍP»C-PrP¶PμPSPSCȚ. PkPμPIC-PrPsPjPs, C±Pë PIPiP»PëPIP°C”
PrCřC,P°CÍC,PμCȚPëPr, C°Ps PiPsC,CȚP°PiPëPi PrPs PsCȚPiP°PSC-P·PjCř P¶C-PSPePë P·
CÍC-PjBȚ™ CȚPj C±PsP»PsPIC-PeP°, CȚPePëPNë P»C-PeCřC”C,CHCÍCȚ P”CřPsPrP°CȚC,PsPj,
PSP° PiP»C-Pr C±PsP»PsPIC-C±PsC— CÍC,P°C,C-.

PİPe C- Cř CȚP°P·C- P·P°CÍC,PsCÍCřPIP°PSPSCȚ C-PSC€PëC... C-PSPiC-P±C-C,PsCȚC-PI 5α-
CȚPμPrCřPeC,P°P·Pë, CȚPμPePsPjPμPSPPrCřC”C,CHCÍCȚ PePsCȚPëCÍC,CřPIP°C,PëCÍCH
PiCȚPμP·PμCȚPIP°C,PëPIPsPj PiC-Pr C±P°CÍ CÍC,P°C,PμPIPsPiPs P°PeC,Cř, CȚPeC°Ps
P¶C-PSPeP° PIP°PiC-C,PSP°, P° C±PsP»PsPIC-Pe P»C-PeCřC”C,CHCÍCȚ P”CřPsPrP°CȚC,PsPj, P·
PjPμC,PsCȚ P·P°PiPsP±C-PiP°PSPSCȚ PiPsC,CȚP°PiP»CȚPSPSCȚ CÍC-PjBȚ™ CȚ PrPs
PsCȚPiP°PSC-P·PjCř P¶C-PSPePë.

PkPμPjP°C” PrPsPeP°P·C-PI C,PsPiPs, C°Ps PIPiPμPrPμPSPSCȚ C,P°PjCÍCřP»PsP·PëPSCř
PiC-PrCȚPsC...P»PsCȚPëPrCř PIP°PiC-C,PSPëPj CÍP°PjPeP°Pj C°CřCȚC-PI C,P° PeCȚPsP»C-PI
Cř PrPsP·P°C..., C°Ps PiPμCȚPμPIPëC°CřCȚC,CH C,PμCȚP°PiPμPIC,PëC±PSC-,
PSPμPiP°C,PëPIPsPs PIPiP»PëPIP°C” PSP° PiP»C-Pr.

P”PsPrCřPIP°PSPSCȚ PiCȚCřPrPrCȚ.

PkPμPIC-PrPsPjPs, C±Pë PiCȚPsPSPëPeP°CȚC,CH PrCřC,P°CÍC,PμCȚPëPr C,P°
C,P°PjCÍCřP»PsP·PëPS Cř PiCȚCřPrPSPμ PjPsP»PsPePs P¶C-PSPePë.

***P—PᵣP°C,PSC-CÍC,CH PIPiP»PëPIP°C,Pë
PSP° C€PIPëPᵣPεC-CÍC,CH
CȚPμP°PeC†C-C— PiCȚPë
PePμCȚC¿PIP°PSPSC-
P°PIC,PsC,CȚP°PSCÍPİPsCȚC,PsPj P°P±Ps
C-PSC€PëPjPë PjPμC...P°PSC-P·PjP°PjPë.***

P”PsCÍP»C-PrP¶PμPSPSCȚ P· PIPëPIC±PμPSPSCȚ PIPiP»PëPICř P”CřPsPrP°CȚC,Cř PSP°
P·PrP°C,PSC-CÍC,CH PePμCȚCřPIP°C,Pë P°PIC,PsC,CȚP°PSCÍPiPsCȚC,PsPj P°P±Ps
C-PSC€PëPjPë PjPμC...P°PSC-P·PjP°PjPë PSPμ PiCȚPsPIPsPrPëP»PëCÍCȚ. PhPrPSP°Pe
PiP°C†C-C”PSC,C-PI PiPsC,CȚC-P±PSPs PiCȚPsC-PSC,,PsCȚPjCřPIP°C,Pë PiCȚPs
PjPsP¶P»PëPIPμ PIPëPSPëPePSPμPSPSCȚ CÍPëPjPiC,PsPjC-PI, PiPsPiBȚ™ CȚP·P°PSPëC... P·
PsCȚC,PsCÍC,P°C,PëC±PSPsCȚ P°CȚC,PμCȚC-P°P»CHPSPsCȚ PiC-PiPsC,PμPSP·C-C”CȚ,

$P \cdot PsPeC_{\overline{H}}P_{\overline{u}}P_jP^\circ$ $\overline{P}iC_{\overline{H}}Ps$ $P \cdot P^\circ \overline{P}iP^\circ P_jPsC_{\overline{H}}PsC_{\overline{+}}P_{\overline{u}}PSPSC_{\overline{u}}$, $\overline{P}iC_{\overline{H}}P_{\overline{e}} P \cdot P^\circ C_{\overline{f}}C$, $PsC_{\overline{f}}C_{\overline{f}}PIP^\circ PSPSC-$
 $P''C_{\overline{f}}PsPrP^\circ C_{\overline{H}}C$, $C_{\overline{f}}$.

$\overline{P}Y\overline{P}iPsC_{\overline{f}}C-P_{\pm} P \cdot P^\circ C_{\overline{f}}C$, $PsC_{\overline{f}}C_{\overline{f}}PIP^\circ PSPSC_{\overline{u}}$ C , $P^\circ PrPsP \cdot P_{\overline{e}}$.

$P''PsC_{\overline{H}}PsC_{\overline{f}}P_{\overline{u}}C-$ ($PIP_{\overline{e}}P_{\overline{u}}C_{\overline{H}}C_{\overline{+}}P^\circ C_{\overline{H}}C_{\overline{+}}P_{\overline{e}} C \dots PIPsC_{\overline{H}}P_{\overline{e}}C \dots P_{\overline{u}}C-C$, $PsC_{\overline{H}}PsPiPs PIC-PeC_{\overline{f}}$)

$P P_{\overline{u}}PePsP_jP_{\overline{u}}PSPPrPsPIP^\circ PSP^\circ PrPsP \cdot P^\circ P''C_{\overline{f}}PsPrP^\circ C_{\overline{H}}C$, $C_{\overline{f}}$ $\overline{b}_{\overline{H}}''$ $1 PeP^\circ \overline{P}iC_{\overline{f}}C_{\overline{f}}P_{\overline{u}}P^\circ$ ($0,5 P_jPi/0,4 P_jPi$) $PSP^\circ PrPsP_{\pm}C_{\overline{f}}$. $P_{\overline{u}}C_{\overline{H}}P_{\overline{u}}\overline{P}iP^\circ C_{\overline{H}}P^\circ C$, $\overline{P}iC_{\overline{H}}P_{\overline{e}}PN_{\overline{e}}P_jP^\circ C_{\overline{H}}C$, $CH_{\overline{H}}$ $\overline{P}iP_{\overline{u}}C_{\overline{H}}PsC_{\overline{H}}P^\circ P_{\overline{u}}CH_{\overline{H}}PSPs$
 $C_{\overline{+}}P_{\overline{u}}C_{\overline{H}}P_{\overline{u}}P \cdot 30 C \dots PIP_{\overline{e}}P_{\overline{u}}P_{\overline{e}}PS \overline{P}iC-C_{\overline{f}}P_{\overline{u}}C_{\overline{u}}$ $C_{\overline{f}}\overline{P}iPsP_{\overline{u}}\overline{P}iPIP^\circ PSPSC_{\overline{u}}$ $C-P_{\overline{u}}C-$ $PI PsPrP_{\overline{e}}PS C-$
 C , $PsPN_{\overline{e}} P_{\overline{u}}P_{\overline{u}} C_{\overline{+}}P^\circ C_{\overline{f}}$. $P_{\overline{u}}P^\circ \overline{P}iC_{\overline{f}}C_{\overline{f}}P_{\overline{u}}C_{\overline{f}} C_{\overline{f}}P_{\overline{u}}C-P_{\overline{r}} PePsPIC$, $P^\circ C$, $P_{\overline{e}} C_{\overline{+}}C-P_{\overline{u}}PsC_{\overline{H}}$, $PSP_{\overline{u}}$
 $PIC-PrPeC_{\overline{H}}P_{\overline{e}}PIP^\circ C$, $P_{\overline{e}} C$, $P^\circ PSP_{\overline{u}}$ $C_{\overline{H}}PsP \cdot P_{\overline{u}}PsPIC_{\overline{f}}PIP^\circ C$, $P_{\overline{e}}$, $PsC_{\overline{f}}PeC-P_{\overline{u}}CH_{\overline{H}}PeP_{\overline{e}} \overline{P}iC_{\overline{H}}P_{\overline{e}}$
 $PePsPSC$, $P^\circ PeC$, $C-$ $C-P$. $PIP_jC-C_{\overline{f}}C$, $PsP_j PeP^\circ \overline{P}iC_{\overline{f}}C_{\overline{f}}P_{\overline{u}}P_{\overline{e}} P_jPsP_{\overline{u}}P_{\overline{u}}P_{\overline{e}}PIP_{\overline{u}}$
 $\overline{P}iPsPrC_{\overline{H}}P^\circ P \cdot PSP_{\overline{u}}PSPSC_{\overline{u}}$ $C_{\overline{f}}P_{\overline{u}}P_{\overline{e}}P \cdot PsPIP_sC-$ $PsP_{\pm}PsP_{\overline{u}}PsPSPeP_{\overline{e}} C_{\overline{H}}PsC$, $P^\circ C$, $P^\circ PiP_{\overline{u}}PsC$, $PeP_{\overline{e}}$.

$P''C_{\overline{f}}PsPrP^\circ C_{\overline{H}}C$, $P_jPsP_{\overline{u}}PSP^\circ P \cdot P^\circ C_{\overline{f}}C$, $PsC_{\overline{f}}PsPIC_{\overline{f}}PIP^\circ C$, $P_{\overline{e}}$ $PrP_{\overline{u}}C_{\overline{u}}$ $P \cdot P^\circ P_jC-C_{\overline{u}}P_{\overline{u}}PSPSC_{\overline{u}}$
 $PePsP_jP_{\pm}C-PSPsPIP^\circ PSPsC-$ C , $P_{\overline{u}}C_{\overline{H}}P^\circ \overline{P}iC-C-$ $PrC_{\overline{f}}C$, $P^\circ C_{\overline{f}}C$, $P_{\overline{u}}C_{\overline{H}}P_{\overline{e}}PrPsP_j C$, P°
 C , $P^\circ P_jC_{\overline{f}}C_{\overline{f}}P_{\overline{u}}PsP \cdot P_{\overline{e}}PSC_{\overline{f}}$ $PiC-PrC_{\overline{H}}PsC \dots P_{\overline{u}}PsC_{\overline{H}}P_{\overline{e}}PrPsP_j P \cdot P_jP_{\overline{u}}C$, $PsC_{\overline{H}}$ $\overline{P}iPsP_{\overline{u}}P_{\overline{u}}PiC_{\overline{e}}P_{\overline{u}}PSPSC_{\overline{u}}$
 $P_{\overline{u}}C-PeC_{\overline{f}}PIP^\circ PSPSC_{\overline{u}}$.

$P-P^\circ P_jC-PSP^\circ P''C_{\overline{f}}PsPrP^\circ C_{\overline{H}}C$, $PsP_jB PrC_{\overline{f}}C$, $P^\circ C_{\overline{f}}C$, $P_{\overline{u}}C_{\overline{H}}P_{\overline{e}}PrC_{\overline{f}} P^\circ P_{\pm}Ps$
 C , $P^\circ P_jC_{\overline{f}}C_{\overline{f}}P_{\overline{u}}PsP \cdot P_{\overline{e}}PSC_{\overline{f}}$ $PiC-PrC_{\overline{H}}PsC \dots P_{\overline{u}}PsC_{\overline{H}}P_{\overline{e}}PrC_{\overline{f}}$ $\overline{P}iC_{\overline{H}}P_{\overline{e}} P_jPsPSPsC$, $P_{\overline{u}}C_{\overline{H}}P^\circ \overline{P}iC-C-$
 $P_jPsP_{\overline{u}}P_{\overline{u}}P_{\overline{e}}PIP^\circ$, $C_{\overline{u}}PeC_{\overline{u}}Ps C_{\overline{+}}P_{\overline{u}} PeP_{\overline{u}}C-PSC-C_{\overline{+}}PSPs PsP_{\pm}T'C_{\overline{H}}C_{\overline{f}}PSC$, $PsPIP^\circ PSPs$.

$\overline{P}K_{\overline{e}}C_{\overline{H}}PePsPIP^\circ PSP_{\overline{u}}PrPsC_{\overline{f}}C$, $P^\circ C$, $PSC-C_{\overline{f}}C$, $CH_{\overline{H}}$

$P_{\overline{u}}P^\circ C_{\overline{H}}P_jP^\circ PePsPeC-PSP_{\overline{u}}C$, $P_{\overline{e}}PeP^\circ P''C_{\overline{f}}PsPrP^\circ C_{\overline{H}}C$, $C_{\overline{f}}$ $C_{\overline{f}}$ $C \dots PIPsC_{\overline{H}}P_{\overline{e}}C \dots P \cdot PSP_{\overline{e}}C_{\overline{H}}PePsPIP_sC_{\overline{H}}$
 $PSP_{\overline{u}}PrPsC_{\overline{f}}C$, $P^\circ C$, $PSC-C_{\overline{f}}C$, $CH_{\overline{H}}$ $PSP_{\overline{u}}$ $PIP_{\overline{e}}PIC_{\overline{+}}P^\circ P_{\overline{u}}P^\circ C_{\overline{f}}CH_{\overline{H}}$. $P-P_jC-PSC_{\overline{H}}PIP^\circ C$, $P_{\overline{e}}$ $PrPsP \cdot C_{\overline{f}}$
 $\overline{P}iC_{\overline{H}}P_{\overline{u}}\overline{P}iP^\circ C_{\overline{H}}P^\circ C$, $C_{\overline{f}}P_{\overline{u}}C_{\overline{u}}$ $P_{\overline{u}}C-PeC_{\overline{f}}PIP^\circ PSPSC_{\overline{u}}$ C , $P^\circ PeP_{\overline{e}}C \dots C \dots PIPsC_{\overline{H}}P_{\overline{e}}C \dots PSP_{\overline{u}}$
 $\overline{P}iPsC$, $C_{\overline{H}}C-P_{\pm}PSPs$ ($PrP_{\overline{e}}PI$. $C_{\overline{H}}PsP \cdot PrC-P_{\overline{u}}$ $B \ll PhC_{\overline{f}}PsP_{\pm}P_{\overline{u}}P_{\overline{e}}PIP_sC_{\overline{f}}C$, $C-$
 $P \cdot P^\circ C_{\overline{f}}C$, $PsC_{\overline{f}}C_{\overline{f}}PIP^\circ PSPSC_{\overline{u}}B \gg C$, $P^\circ B \ll P_{\overline{u}}P^\circ C_{\overline{H}}P_jP^\circ PePsPeC-PSP_{\overline{u}}C$, $P_{\overline{e}}PeP^\circ B \gg$).

$\overline{P}_{\overline{u}}P_{\overline{u}}C_{\overline{+}}C-PSPePsPIP^\circ PSP_{\overline{u}}PrPsC_{\overline{f}}C$, $P^\circ C$, $PSC-C_{\overline{f}}C$, $CH_{\overline{H}}$

$P_{\overline{u}}P^\circ C_{\overline{H}}P_jP^\circ PePsPeC-PSP_{\overline{u}}C$, $P_{\overline{e}}PeP^\circ P''C_{\overline{f}}PsPrP^\circ C_{\overline{H}}C$, $C_{\overline{f}}$ $C_{\overline{f}}$ $C \dots PIPsC_{\overline{H}}P_{\overline{e}}C \dots P \cdot$
 $\overline{P}iP_{\overline{u}}C_{\overline{+}}C-PSPePsPIP_sC_{\overline{H}}$ $PSP_{\overline{u}}PrPsC_{\overline{f}}C$, $P^\circ C$, $PSC-C_{\overline{f}}C$, $CH_{\overline{H}}$ $PSP_{\overline{u}}$ $PIP_{\overline{e}}PIC_{\overline{+}}P^\circ P_{\overline{u}}P^\circ C_{\overline{f}}CH_{\overline{H}}$, C , $PsP_jC_{\overline{f}}$
 $\overline{P}iC_{\overline{H}}P_{\overline{u}}\overline{P}iP^\circ C_{\overline{H}}P^\circ C$, $C_{\overline{f}}P_{\overline{u}}C_{\overline{u}}$ $P_{\overline{u}}C-P_{\overline{r}} P \cdot P^\circ C_{\overline{f}}C$, $PsC_{\overline{f}}PsPIC_{\overline{f}}PIP^\circ C$, $P_{\overline{e}}$ $P \cdot PsP_{\pm}P_{\overline{u}}C_{\overline{H}}P_{\overline{u}}P_{\overline{u}}PSC-C_{\overline{f}}C$, $CH_{\overline{H}}$
 $\overline{P}iC_{\overline{H}}P_{\overline{e}} P_{\overline{u}}P_{\overline{u}}PiPeC-PN_{\overline{e}} C$, $P^\circ \overline{P}iPsP_jC-C_{\overline{H}}PSC-PN_{\overline{e}}$ $\overline{P}iP_{\overline{u}}C_{\overline{+}}C-PSPePsPIC-PN_{\overline{e}}$
 $PSP_{\overline{u}}PrPsC_{\overline{f}}C$, $P^\circ C$, $PSPsC_{\overline{f}}C$, $C-$ ($PrP_{\overline{e}}PI$. $C_{\overline{H}}PsP \cdot PrC-P_{\overline{u}}$ $B \ll PhC_{\overline{f}}PsP_{\pm}P_{\overline{u}}P_{\overline{e}}PIP_sC_{\overline{f}}C$, $C-$
 $P \cdot P^\circ C_{\overline{f}}C$, $PsC_{\overline{f}}C_{\overline{f}}PIP^\circ PSPSC_{\overline{u}}B \gg C$, $P^\circ B \ll P_{\overline{u}}P^\circ C_{\overline{H}}P_jP^\circ PePsPeC-PSP_{\overline{u}}C$, $P_{\overline{e}}PeP^\circ B \gg$). $\overline{P}iPIP_sC_{\overline{H}}P_{\overline{e}}P_j P \cdot$
 C , $C_{\overline{u}}P_{\overline{u}}PePsC_{\overline{H}}$ $\overline{P}iP_{\overline{u}}C_{\overline{+}}C-PSPePsPIP_sC_{\overline{H}}$ $PSP_{\overline{u}}PrPsC_{\overline{f}}C$, $P^\circ C$, $PSC-C_{\overline{f}}C$, $CH_{\overline{H}}$ $\overline{P}iC_{\overline{H}}P_{\overline{u}}\overline{P}iP^\circ C_{\overline{H}}P^\circ C$,
 $\overline{P}iC_{\overline{H}}PsC$, $P_{\overline{e}}\overline{P}iPsPeP^\circ P \cdot P^\circ PSP_{\overline{e}}PN_{\overline{e}}$ ($PrP_{\overline{e}}PI$. $C_{\overline{H}}PsP \cdot PrC-P_{\overline{u}}$ $B \ll P_{\overline{u}}C_{\overline{H}}PsC$, $P_{\overline{e}}\overline{P}iPsPeP^\circ P \cdot P^\circ PSPSC_{\overline{u}}B \gg$).

$P''C-C$, $P_{\overline{e}}$. B

$P-P^\circ C_{\overline{f}}C$, $PsC_{\overline{f}}C_{\overline{f}}PIP^\circ PSPSC_{\overline{u}}$ $\overline{P}iC_{\overline{H}}PsC$, $P_{\overline{e}}\overline{P}iPsPeP^\circ P \cdot P^\circ PSPs$.

$\overline{P}_{\overline{u}}P_{\overline{u}}C_{\overline{H}}P_{\overline{u}}PrPsP \cdot C_{\overline{f}}PIP^\circ PSPSC_{\overline{u}}$.

P"°PSPëC... PïCḡPs PIPëPï°PrPePë PïPµCḡPµPrPsP·CḡPIP°PSPSCḡ P"ḡPsPrP°CḡC,PsPj
PSPµPjP°C". P"°P»C- PSP°PrP°C"C,CHCḡCḡ C-PSC,,PsCḡPjP°CḡC-Cḡ PïCḡPs
P·P°CḡC,PsCḡCḡPIP°PSPSCḡ PePsP¶PSPsPiPs PePsPjPïPsPSPµPSC,P° PsPeCḡPµPjPs.

P"ḡCḡC,P°CḡC,PµCḡPëPr

P—P° PrP°PSPëPjPë PeP»C-PSC-CḡPSPëC... PrPsCḡP»C-PrP¶PµPSCḡ, Cḡ
PrPsP±CḡPsPIPsP»CHCḡC-PI CḡP°P·PsPIC- PrPsP·Pë PrCḡC,P°CḡC,PµCḡPëPrCḡ PrPs 40
PjPi/PrPsP±Cḡ (CḡB 80 CḡP°P·C-PI PIPëC%oC- P·P° C,PµCḡP°PïPµPIC,PëCḡPSC-)
PïCḡPsC,CḡPiPsPj 7 PrPSC-PI PSPµ PIPëPeP»PëPeP°P»Pë P·P°PSPµPïPsPePsC"PSCḡ C%oPsPrPs
P±PµP·PïPµPePë C—C... P·P°CḡC,PsCḡCḡPIP°PSPSCḡ. PµC-Pr CḡP°Cḡ PeP»C-PSC-CḡPSPëC...
PrPsCḡP»C-PrP¶PµPSCḡ P·P°CḡC,PsCḡPsPICḡPIP°P»Pë PrPsP·Pë PrCḡC,P°CḡC,PµCḡPëPrCḡ PïPs
5 PjPi/PrPsP±Cḡ PïCḡPsC,CḡPiPsPj 6 PjC-CḡCḡCḡC-PI P±PµP· PïPsCḡPIPë
PrPsPrP°C,PePsPIPëC... PïPsP±C-CḡPSPëC... CḡPµP°PeCḡC-PNḡ PïPsCḡC-PIPSCḡPSPs C-P·
P·P°CḡC,PsCḡCḡPIP°PSPSCḡPj PrCḡC,P°CḡC,PµCḡPëPrCḡ Cḡ PrPsP·C- 0,5 PjPi/PrPsP±Cḡ.

PŸPïPµCḡPëC,,C-CḡPSPsPiPs P°PSC,PëPrPsC,Cḡ PSPµPjP°C", C,PsPjCḡ Cḡ CḡP°P·C-
PjPsP¶P»PëPIPsPiPs PïPµCḡPµPrPsP·CḡPIP°PSPSCḡ PïCḡPsPIPsPrCḡC,CH
CḡPëPjPiC,PsPjP°C,PëCḡPSCḡ C,P° PïC-PrC,CḡPëPjCḡPIP°P»CHPSCḡ C,PµCḡP°PïC-Cḡ.

PjP°PjCḡCḡP»PsP·PëPS

PḡP°PrC...PsPrPëP»Pë PïPsPIC-PrPsPjP»PµPSPSCḡ C%oPsPrPs PïPsCḡC,CḡPsPiPs
PïPµCḡPµPrPsP·CḡPIP°PSPSCḡ C,P°PjCḡCḡP»PsP·PëPSCḡ PïC-PrCḡPsC...P»PsCḡPëPrPsPj Cḡ
PrPsP·C- 5 PjPi, PIB CḡPµP·CḡP»CHC,P°C,C-B CḡPePsPiPsB
CḡPïPsCḡC,PµCḡC-PiP°P»P°CḡCHB PïPsCḡC,CḡP°B P°CḡC,PµCḡC-P°P»CHPSP°B
PiC-PïPsC,PµPSP·C-CḡB (CḡPëCḡC,PsP»C-CḡPSPëPNḡ B P°CḡC,PµCḡC-P°P»CHPSPëPNḡB
C,PëCḡPe 70 PjPj/Hg), P±P»CHPIP°PSPSCḡ C,P° PrC-P°CḡPµCḡ, CḡPeC- P»C-PeCḡPIP°P»Pë
C-PSC,,CḡP·C-C"ḡ CḡC-PrPëPSPë, PïC-CḡP»Cḡ CḡPsPiPs PïP°CḡC-C"PSC, PIC-PrCḡCḡPI
PïPsP»PµPiC¶PµPSPSCḡ Cḡ C,PsPNḡ CḡP°PjPëPNḡ PrPµPSCḡ. Pj CḡP°P·C- PïPsCḡC,CḡPsC—
P°CḡC,PµCḡC-P°P»CHPSPsC— PiC-PïPsC,PµPSP·C-C—, CḡPeP° PIPëPSPëPeP°C" PïC-CḡP»Cḡ
PïPµCḡPµPrPsP·CḡPIP°PSPSCḡ C,P°PjCḡCḡP»PsP·PëPSCḡ PïC-PrCḡPsC...P»PsCḡPëPrPsPj,
CḡP»C-Pr P·P°P±PµP·PïPµCḡPëC,Pë PïC-PrC,CḡPëPjPeCḡ PrC-CḡP»CHPSPsCḡC,C-
CḡPµCḡCḡPµPIPs-CḡCḡPrPëPSPSPsC— CḡPëCḡC,PµPjPë. PµP°CḡC-C"PSC,Cḡ PI C,P°PePsPjCḡ
CḡC,P°PSC- CḡP»C-Pr PïCḡPëPNḡPSCḡC,Pë PïPsCḡPëP·PsPSC,P°P»CHPSPµ
PïPsP»PsP¶PµPSPSCḡ, C%oPsP± PIC-PrPSPsPIPëC,Pë P°CḡC,PµCḡC-P°P»CHPSPëPNḡ C,PëCḡPe
C- PSPsCḡPjP°P»C-P·CḡPIP°C,Pë CḡP°CḡC,PsC,Cḡ CḡPµCḡCḡPµPIPëC... CḡPePsCḡPsCḡPµPSCḡ.
PïPeC%oPs CḡPµ PSPµ PrPsPïPsPjPsP¶Pµ, CḡP»C-Pr PïCḡPëP·PSP°CḡPëC,Pë
PïP»P°P·PjPsP·P°PjC-PSPSPëPePë, P° Cḡ CḡP°P·C- PSPµPsP±C...C-PrPSPsCḡC,C- ḡḡ"
CḡCḡPrPëPSPsP·PICḡP¶CḡPIP°P»CHPSC- P·P°CḡPsP±Pë. PµPsC,CḡC-P±PSPs CḡC,PµP¶PëC,Pë
P·P° C,,CḡPSPeCḡC-C"ḡ PSPëCḡPsPe C- PïCḡPsPIPsPrPëC,Pë
P·P°PiP°P»CHPSPsPïC-PrC,CḡPëPjCḡPIP°P»CHPSCḡ C,PµCḡP°PïC-Cḡ. P"ḡC-P°P»C-P· PjPsP¶Pµ
PIPëCḡPIPëC,PëCḡCḡ PSPµPµC,,PµPeC,PëPIPSPëPj, PsCḡPeC-P»CHPePë
C,P°PjCḡCḡP»PsP·PëPSCḡ PïC-PrCḡPsC...P»PsCḡPëPr PjP°PNḡP¶Pµ PïPsPIPSC-CḡC,Cḡ
P·PiBḡ™ CḡP·CḡC"C,CHCḡCḡ P· P±C-P»PeP°PjPë PïP»P°P·PjPë.

PµCḡPë PïPµCḡPµPrPsP·CḡPIP°PSPSC-, C%oPsP± P·P°PïPsP±C-PiC,Pë P°P±CḡPsCḡP±CḡC-C—,
Cḡ PïP°CḡC-C"PSC,P° PSPµPsP±C...C-PrPSPs PIPëPeP»PëPeP°C,Pë P±P»CHPIP°PSPSCḡ.
PïPeC%oPs PïCḡPëPNḡPSCḡC,Ps PIPµP»PëPeC- PrPsP·Pë PïCḡPµPïP°CḡP°C,Cḡ,
PSPµPsP±C...C-PrPSPs PïCḡPsPIPµCḡC,Pë PïCḡPsPjPëPIP°PSPSCḡ C¶P»CḡPSPeP°, PrP°C,Pë
P°PeC,PëPIPsPIP°PSPµ PICḡPiC-P»P»Cḡ C,P° PïCḡPsPSPsCḡPSPµ, PSP°PïCḡPëPeP»P°Pr
CḡCḡP»CHC,,P°C, PSP°C,CḡC-Cḡ.

РμРѕР±С-С‡РѕС- СЃРμР°РєС†С-С—.

РЉР»С-РѕС-С‡РѕС- РrPsCfP»С-РrP¶PμPSPSC¶ P·Р°CfC,PsCfCfPIP°PSPSC¶ P”CfPsPrP°CЃC,Cf PSPμ PīCЃPsPIPсPrPёP»PёCfC¶, PsPrPSP°Pe P±CfP»Ps PīCЃPsPrPμPjPsPSCfC,CЃPsPIP°PSPs P±C-PsPμPePIC-PIP°P»PμPSC,PSC-CfC,CH P”CfPsPrP°CЃC,Cf PīCЃPё CfCfPjC-CfPSPsPjCf P·Р°CfC,PsCfCfPIP°PSPSC- РrCfC,Р°CfC,PμCЃPёPrCf C,Р° C,Р°PjCfCfP»PsP·PёPSCf. P†PSC,,PsCЃPjP°C†C-СЃ PīCЃPs PsPrPSPсC‡P°CfPSPμ P·Р°CfC,PsCfCfPIP°PSPSC¶ PsPrPμCЃP¶P°PSPs P· РrPsCfP»С-РrP¶PμPSPSC¶ CombAT (PePsPjP±C-PSP°C†C-С¶ PЃPIPсPrP°CЃC,Cf C,Р° C,Р°PjCfCfP»PsP·PёPSCf), PI C¶PePsPjCf PīPsCЃC-PIPSCЃPIP°P»Pё PePsPjP±C-PSP°C†C-СЃ РrCfC,Р°CfC,PμCЃPёPrCf PI РrPsP·C- 0,5 PjPi C,Р° C,Р°PjCfCfP»PsP·PёPSCf 0,4 PjPi PsPrPёPS CЃP°P· PSP° РrPsP±Cf PīCЃPsC,C¶PiPsPj 4 CЃPsPeC-PI P°P±Ps PjPsPSPсC,PμCЃP°PiC-СЃ C†PёPjPё PīCЃPμPīP°CЃP°C,Р°PjPё.

P†PSC,,PsCЃPjP°C†C-СЃ PīCЃPs PīPsP±C-С‡РѕС- СЃРμР°РєС†С-С— PePsP¶PSPsPiPs PePsPjPiPsPSPμPSC,Р° PsPeCЃPμPjPs (РrCfC,Р°CfC,PμCЃPёPr C,Р° C,Р°PjCfCfP»PsP·PёPS) C,Р°PePsP¶ PSP°PIPμPrPμPSPs PSPёP¶C‡Pμ. PкPμ PīCЃPs PICfC- PīPsP±C-С‡РѕС- СЃРμР°РєС†С-С—, C%Ps PIC-РrPjC-С‡P°P»Pё PīCЃPё P·Р°CfC,PsCfCfPIP°PSPSC- PePsP¶PSPsPiPs PePsPjPiPsPSPμPSC,Р° PsPeCЃPμPjPs, PīPsPIC-РrPsPjP»C¶P»Pё PīCЃPё P·Р°CfC,PsCfCfPIP°PSPSC- P”CfPsPrP°CЃC,Cf, C- C,PsPjCf C-PSC,,PsCЃPjP°C†C-СЃ PīCЃPs PīPsP±C-С‡РѕС- СЃРμР°РєС†С-С— PīCЃPё P·Р°CfC,PsCfCfPIP°PSPSC- PsPeCЃPμPjPёC... PePsPjPiPsPSPμPSC,C-PI P”CfPsPrP°CЃC,Cf C,Р°PePsP¶ PIPeP»СЃC‡PμPSPs PI РrP°PSCf C-PSCfC,CЃCfPeC†C-СЃ.

P—Р° РrP°PSPёPjPё 4-СЃC-С‡PSPsPiPs РrPsCfP»С-РrP¶PμPSPSC¶ CombAT, PIC-РrCfPsC,PsPe PīPsP±C-С‡PSPёC... СЃРμР°РєС†С-PNё, PIPёP·PSP°C‡PμPSPёC... РrPsCfP»С-РrPSPёPeP°PjPё PīCЃPsC,C¶PiPsPj PīPμCЃCёPsPiPs, РrCЃCfPiPsPiPs, C,CЃPμC,CHPsPiPs C,Р° C‡PμC,PIPμCЃC,PsPiPs CЃPsPeC-PI P»C-РєCfPIP°PSPSC¶, P·PjC-PSCЃPIP°PICfC¶: PIC-РrPīPsPIC-РrPSPs 22 %, 6 %, 4 % C,Р° 2 % PīCЃPё PePsPjP±C-PSPsPIP°PSC-PNё C,PμCЃP°PiC-С— РrCfC,Р°CfC,PμCЃPёPr C,Р°PjCfCfP»PsP·PёPS; 15 %, 6 %, 3 % C,Р° 2 %B PīCЃPё PjPsPSPсC,PμCЃP°PiC-С— РrCfC,Р°CfC,PμCЃPёPrPsPj; 13 %, 5 %, 2 %, C,Р° 2 % PīCЃPё PjPsPSPсC,PμCЃP°PiC-С— C,Р°PjCfCfP»PsP·PёPSPsPj. P’PёC%PёPNё PIC-РrCfPsC,PsPe PīPsP±C-С‡PSPёC... СЃРμР°РєС†С-PNё Cf PīCЃCfPiC-, C¶PeP° PsC,CЃPёPjCfPIP°P»P° PePsPjP±C-PSPsPIP°PSCf C,PμCЃP°PiC-СЃ, PīCЃPsC,C¶PiPsPj PīPμCЃCёPsPiPs CЃPsPeCf P»C-РєCfPIP°PSPSC¶ P·CfPjPsPIP»PμPSPёPNё PIPёC%PёPjPё PīPsPeP°P·PSPёPeP°PjPё CЃPμPīCЃPsPrCfPeC,PёPIPSPёC... PīPsCЃCfCёPμPSCЃ, Р° CfP°PjPμ PīPsCЃCfCёPμPSPSC¶ PμC¶PeCfP»C¶C†C-С—, C¶PeC- CfPīPsCfC,PμCЃC-PiP°P»PёCfCH Cf PīCЃCfPiC-.

PμPsP±C-С‡РѕС- СЃРμР°РєС†С-С—, C%Ps PIPёPSPёPeP°P»Pё P· C‡P°CfC,PsC,PsCHB ≥1 % PīCЃPsC,C¶PiPsPj PīPμCЃCёPsPiPs CЃPsPeCf P·Р°CfC,PsCfCfPIP°PSPSC¶, P·Р° РrP°PSPёPjPё РrPsCfP»С-РrPSPёC†CHPePёC... P°PSP°P»C-P·C-PI CombAT, REDUCE, Р° C,Р°PePsP¶ PeP»C-PSC-С‡PSPёC... РrPsCfP»С-РrP¶PμPSCЃ PjPsPSPсC,PμCЃP°PiC-PNё PePsPjPiPsPSPμPSC,Р°PjPё P”CfPsPrP°CЃC,Cf, PSP°PIPμPrPμPSC- PI C,Р°P±P»PёC†C-.

P†PSC,,PsCЃPjP°C†C-С¶ C%PsPrPs PīPsP±C-С‡PSPёC... СЃРμР°РєС†С-PNё C,Р°PjCfCfP»PsP·PёPSCf P±P°P·CfC”C,CHCfC¶ PSP° РrP°PSPёC..., C%Ps РrPsCfC,CfPīPSC- PSP° PIC-РrPīPsPIC-РrPSPёC... PjPμPrPёC‡PSPёC... СЃРμР°CfCfCЃCfP°C.... PЃP°CfC,PsC,Р° C—C... PIPёPSPёPePSPμPSPSC¶ PjPsP¶Pμ P·CЃPsCfC,Р°C,Pё PīCЃPё PsPrPSPсC‡P°CfPSPsPjCf P·Р°CfC,PsCfCfPIP°PSPSC- РrCfC,Р°CfC,PμCЃPёPrCf C,Р° C,Р°PjCfCfP»PsP·PёPSCf.

P\$P°CfC,PsC,P° PIPëPSPëPePSPµPSPSCl PİPsP±C-C±PSPëC... CĤPµP°PeC†C-PNē,
PIPëCłIPIP»PµPSPëC... Cr PeP»C-PSC-C±PSPëC... PrPsCłP»C-PrP¶PµPSPSClC...: C±P°CfC,Ps (≥
1/100 B B-B B B B B B B B < 1/10), PSPµC±P°CfC,PsB (≥ 1/1000 B- B < 1/100), CĤC-PrPePs (≥
1/10000 B- B < 1/1000), PrCfP¶Pµ CĤC-PrPePs (< 1/10000). PµPsP±C-C±PSC- CĤPµP°PeC†C-C—,
PeP»P°CłPëC„C-PePsPIP°PSC- P·P° PeP»P°CłP°PjPë CłPëCłC,PµPj PsCĤPiP°PSC-PI,
PİCĤPµPrCłC,P°PIP»PµPSPs Cr PİPsCĤCłIPrPeCr P·PSPëP¶PµPSPSCl C—C... CfC,CfPİPµPSCl
C,CłP¶PePsCłC,C-.

PµP»P°Cł CłPëCłC,PµPjPë PsCĤPiP°PSC-PI	PµPsP±C-C±PSC- CĤPµP°PeC†C-C—	P”CfC,P°CfC,PµCĤPëPr C,P°PjCłCfP»PsP·PëPS	P”CfC,P°CfC,PµCĤPëPr	PÿP°PjCłCfP»PsP·PëPS
P— P±PsPeCf PSPµCĤPIPSPsC— CłPëCłC,PµPjPë	PkPµPİCĤPëC,PsPjPSC-CłC,CH P—P°PİP°PjPsCĤPsC†PµPSPSCl P”PsP»PsPIPSPëPNē P±C-P»CH	- P\$P°CfC,Ps -	-	P C-PrPePs P\$P°CfC,Ps PkPµC±P°CfC,Ps
P— P±PsPeCf CłPµCĤC†Cł	B PÿPµCĤC†PµPIP° PSPµPrPsCłC,P°C,PSC-CłC,CH (P·P±C-CĤPSPµ PİPsPSClC,C,Cł¹) PµPsCłPëP»PµPSPµ CłPµCĤC†PµP±PëC,C,Cł	PkPµC±P°CfC,Ps	PkPµC±P°CfC,Ps ^d	-
P— P±PsPeCf CłCfPrPëPSPSPsC— CłPëCłC,PµPjPë	PµPsCłC,CfCĤP°P»CHPSP° PİC-PİPsC,PµPSP·C-Cł	-	-	PkPµC±P°CfC,Ps
P— P±PsPeCf PrPëC...P°P»CHPSPsC— CłPëCłC,PµPjPë, PsCĤPiP°PSC-PI PİCĤCfPrPSPsC— PeP»C-C,PëPë C-B CłPµCĤPµPrPsCłC,C-PSPSCl	P PëPSC-C,	-	-	PkPµC±P°CfC,Ps
P— P±PsPeCf CëP»CfPSPePsIPs- PePëCëPePsIPsPİPs C,CĤP°PeC,Cf	P—P°PİPsCĤ P”C-P°CĤPµCł PkCfPrPsC,P° P”P»CĤPIP°PSPSCl	- - - -	-	PkPµC±P°CfC,Ps PkPµC±P°CfC,Ps PkPµC±P°CfC,Ps PkPµC±P°CfC,Ps
P— P±PsPeCf CëPeC-CĤPë C,P° PİC-PrCëPeC-CĤPSPëC... C,PeP°PSPëPS	PĥPSPİC-PsPSPµPICĤPsC,PëC†PSPëPNē- PSP°P±CĤCłPe PÿPëPSPrCĤPsPj PÿC,C-PIPµPSCłP° BĤ” P”P¶PsPSCłPsPSP° PµCĤPsPİPëPİCłPSPeP° P”PëCłPëPİ PÿPIPµCĤP±C-P¶	- - - - - -	-	P C-PrPePs P”CfP¶Pµ CĤC-PrPePs PkPµC±P°CfC,Ps PkPµC±P°CfC,Ps PkPµC±P°CfC,Ps
P— P±PsPeCf CĤPµPİCĤPsPrCfPeC,PëPIPSPsC— CłPëCłC,PµPjPë C- PİCĤCfPrPSPëC... P·P°P»PsP·	PµCĤC-P°PİC-P·Pj P†PjPİPsC,PµPSC†C-Cł³ PµPsCĤCfCëPµPSPSCl³ (P·PSPëP¶PµPSPSCl) P»C-P±C-PrPs PµPsCĤCfCëPµPSPSCl³~ PµCłPeCfP»CłC†C-C— P—P°C...PIPSCĤPİP°PSPSCl PİCĤCfPrPSPëC... P·P°P»PsP·²	- P\$P°CfC,Ps P\$P°CfC,Ps P\$P°CfC,Ps P\$P°CfC,Ps P\$P°CfC,Ps	P\$P°CfC,Ps ^b P\$P°CfC,Ps ^b P\$P°CfC,Ps ^b P\$P°CfC,Ps ^b	- - - P\$P°CfC,Ps -
P—P°PİP°P»CHPSC- CĤPsP·P»P°PrPë	PĥCłC,PµPSC-Cł	-	-	PkPµC±P°CfC,Ps

aB B B B B B B B B B B B P”CfC,P°CfC,PµCĤPëPr C,P°PjCłCfP»PsP·PëPS:B Cr PrPsCłP»C-PrP¶PµPSPSC-
CombAT C±P°CfC,PsC,P° C†PëC... PİPsP±C-C±PSPëC... CĤPµP°PeC†C-PNē
P·PSPëP¶CfC”C,CHCłCł P· PePsP¶PSPëPj PSP°CfC,CfPİPSPëPj CĤPsPePsPj P· 1-PİPs PrPs 4-PİPs.

bB B B B B B B B B B B P— PrPsCłP»C-PrP¶PµPSCĤ PjPsPSPsC,PµCĤP°PİC-C—
PrPsP±CĤPsCłPeC-CłPSPsC— PİC-PİPµCĤPİP»P°P·C-C— PİPµCĤPµPrPjC-C...CrCĤPsIPsC—
P·P°P»PsP·Pë PrCfC,P°CfC,PµCĤPëPrPsPj.

cB B B B B B B B B B B B P— PsCłPSPsPIPSPsC— C-PSC„PsCĤPjP°C†C-C— P· P±PµP·PİPµPePë
C,P°PjCłCfP»PsP·PëPSCr PrP»Cł PeCĤP°C—PS P·Pÿ.

dB B B B B B B B B B B B P”PsCłP»C-PrP¶PµPSPSCl REDUCE.

¹B B B B B B B B B B B B P—P±C-CĤPSPµ PİPsPSClC,C,Cł B«CłPµCĤC†PµPIP°
PSPµPrPsCłC,P°C,PSC-CłC,CHB» PIPeP»CĤC±P°C” P·P°CfC,C-PNēPSCr CłPµCĤC†PµPICr

PSPμPrPsCfC,P°C,PSC-CfC,CH, CΓPμCḡC†PμPICr PSPμPrPsCfC,P°C,PSC-CfC,CH,
PSPμPrPsCfC,P°C,PSC-CfC,CH P»C-PIPsPiPs C€P»CfPSPsC†PeP°, PiPsCfC,CḡCf
CΓPμCḡC†PμPICr PSPμPrPsCfC,P°C,PSC-CfC,CH, PeP°CḡPrC-PsPiPμPSPSPëPNë C€PsPe,
PiPsCfC,CḡCf PSPμPrPsCfC,P°C,PSC-CfC,CH P»C-PIPsPiPs C€P»CfPSPsC†PeP°,
PSPμPrPsCfC,P°C,PSC-CfC,CH PiCḡP°PIPsPiPs C€P»CfPSPsC†PeP°, PiPsCfC,CḡCf
PSPμPrPsCfC,P°C,PSC-CfC,CH PiCḡP°PIPsPiPs C€P»CfPSPsC†PeP°,
PSPμPrPsCfC,P°C,PSC-CfC,CH C€P»CfPSPsC†PeP°,
PeP°CḡPrC-PsPiC†P»CHPjPsPSP°P»CHPSCr PSPμPrPsCfC,P°C,PSC-CfC,CH,
B P·P°CfC,C-PNëPSCr PeP°CḡPrC-PsPiP°C,C-CH.

2B B B B B B B B B B B B P'PeP»CHC†P°CḡC†Pë PiC-PiPμCḡPμCfC,PμP·C-CH C,P°
P·P±C-P»CHC€PμPSPSCḡ PiCḡCfPrPSPëC... P·P°P»PsP·.

3B B B B B B B B B B B B PiPsP±C-C†PSC- CḡPμP°PeC†C-C—, PiPsPiBḡ™ CḡP·P°PSC- P·
PiPsCḡCfC€PμPSPSCḡPj CΓPμPeCfC†P°P»CHPSPsC— C„CfPSPeC†C-C—,
P°CfPsC†C-CHCHC,CHCfCḡ P· P»C-PeCfPIP°PSPSCḡPj PrCfC,P°CfC,PμCḡPëPrPsPj
(PIPeP»CHC†P°CḡC†Pë PjPsPSPsC,PμCḡP°PiC-CH C,P° PePsPjP±C-PSP°C†C-CH P·
C,P°PjCfC†P»PsP·PëPSPsPj). PiC- PiPsP±C-C†PSC- CḡPμP°PeC†C-C— PjPsP¶CfC,CH
C,CḡPëPIP°C,Pë PiC-CfP»Cḡ PiCḡPëPiPëPSPμPSPSCḡ P»C-PeCfPIP°PSPSCḡ. P'PiP»PëPI
PrCfC,P°CfC,PμCḡPëPrCf PSP° C—C... C,CḡPëPIP°P»C-CfC,CH PSPμPIC-PrPsPjP°.

^B B B B B B B B P'PeP»CHC†P°CḡC†Pë P·PjPμPSC€PμPSPSCḡ PsP±Bḡ™ C" PjCf CΓPiPμCḡPjPë.

P"°PSC- PiPsCfC,PjP°CḡPePμC,PëPSPiPsPIPëC... PrPsCfP»C-PrP¶PμPSCḡ

PJ PiPsCfC,PjP°CḡPePμC,PëPSPiPsPIPsPjCf CΓPiPsCfC,PμCḡPμP¶PμPSPSC- PiPsP±C-C†PSC-
CḡPμP°PeC†C-C— C„C-PeCfC†PIP°P»PëCfCḡ P·C- CΓPiPsPSC,P°PSPSPëC...
PiPsPIC-PrPsPjP»PμPSCḡ, C,PsPjCf C,PsC†PSP° C†P°CfC,PsC,P° C,P°PePëC... CḡPμP°PeC†C-PNë
PSPμPIC-PrPsPjP°.

PḡPsPSPsC,PμCḡP°PiC-Cḡ PrCfC,P°CfC,PμCḡPëPrPsPj

P— P±PsPeCž C-PjCžPSPSPsC— CΓPëCfC,PμPjPë

PŞP°CfC,PsC,P° PSPμPIC-PrPsPjP°: P°P»PμCḡPiC-C†PSC- CḡPμP°PeC†C-C—,
PIPeP»CHC†P°CḡC†Pë PiPëCfPëPi, CΓPIPμCḡP±C-P¶, PeCḡPsPiPëPiBḡ™ CḡPSPeCf,
P»PsPeP°P»C-P·PsPIP°PSPëPNë PSP°P±CḡCḡPe C,P° P°PSPiC-PsPSPμPICḡPsC,PëC†PSPëPNë
PSP°P±CḡCḡPe.

P— P±PsPeCž PiCfPëC...C-PePë

PŞP°CfC,PsC,P° PSPμPIC-PrPsPjP°: PrPμPiCḡPμCfC-Cḡ.

P— P±PsPeCž C€PeC-CḡPë C,P° PiC-PrC€PeC-CḡPSPsC— PeP»C-C,PePsPIPëPSPë

P C-PrPePs: P°P»PsPiPμC†C-Cḡ (PiPsP»PsPIPSPëPj C†PëPSPsPj, PIC,CḡP°C,P° PIPsP»PsCfCfCḡ
PSP° C,C-P»C-), PiC-PiPμCḡC,CḡPëC...PsP·.

P— P±PsPeCž CḡPμPiCḡPsPrCžPeC,PëPIPSPsC— CΓPëCfC,PμPjPë C,P° PiCḡCžPrPSPëC...
P·P°P»PsP·.

$\text{P}\ddot{\text{S}}\text{P}^{\circ}\text{C}\dot{\text{I}}\text{C}, \text{PsC}, \text{P}^{\circ} \text{PSP}_{\mu}\text{PIC}-\text{PrPsPjP}^{\circ}: \text{C}, \mu\text{C}\dot{\text{I}}\text{C}, \text{P}\ddot{\text{e}}\text{PeC}\dot{\text{r}}\text{P}\gg\text{C}\dot{\text{I}}\text{C}\dot{\text{H}}\text{PSP}\ddot{\text{e}}\text{PN}_{\text{e}} \text{P}\pm\text{C}-\text{P}\gg\text{CHb C}, \text{P}^{\circ}$
 $\text{PSP}^{\circ}\text{P}\pm\text{C}\dot{\text{H}}\text{C}\dot{\text{I}}\text{Pe}.$

P_HPsPSPsC,P_uC₇P^oP_iC-C₁₁C,P^oP_jC₁C₁P»PsP·P_ePSPsP_j

P—P° PrP°PSPëPjPë PïPscÍ'C,PjP°CĤjPePμC,PëPSPiPsPIPsPiPs CÍ'PiPsCÍ'C,PμCĤjPμP¶PμPSPSCÍj
PiC—Pr C‡P°CÍ' PsPiPμCĤjP°C†C—C— P· PiCĤjPëPIPsPrCr PeP°C,P°CĤjP°PeC,Pë C,P°
PiP»P°CrPePsPjPë Cr PrPμCÍjPePëC... PiP°C†C—C"PSC,C—PI, CÍjPeC— CĤjP°PSC—C€Pμ
PsC,CĤjPëPjCÍ'PIP°P»Pë P°P»ChC,,P°1—P°PrCĤjPμPSPsP±P»PsPeP°C,PsCĤjPë,
PIPeP»ChC‡P°ChC‡Pë C,P°PjCÍ'CrP»PsP·PëPS, P±CrPI PIC—PrP·PSP°C‡PμPSPëPNë
C—PSC,CĤjP°PsPiPμCĤjP°C†C—PNëPSPëPNë CÍ'PëPSPrCĤjPsPj P°C,PsPSC—C‡PSPsC—
CĤjP°PMëPrCrP¶PePë (P†PŸPĥP , PIP°CĤjC—P°PSC, CÍ'PëPSPrCĤjPsPjCÍ' PIC†P·ChPePsC—
P·C—PSPëC†C—) (PrPëPI. B«PĥCÍ'PsP±P»PëPIPsCÍ'C,C— P·P°CÍ'C,PsCÍ'CrPIP°PSPSCÍjB»).

$\text{P}_{\mu}\text{C}-\text{Pr}\ \text{C}\ddagger\text{P}^{\circ}\text{C}\ddagger\ \text{P}\ddot{\text{C}}-\text{C}\ddagger\text{P}\rangle\text{C}\ddagger\text{C}\ddagger\text{P}_{\mu}\text{C}''\text{C}\ddagger\text{C},\text{C}\ddagger\text{P}^{\circ}\text{C}\ddagger-\text{P}_{\mu}\text{PSPsPiPs}\ \text{P}\cdot\text{P}^{\circ}\text{C}\ddagger\text{C},\text{PsC}\ddagger\text{C}\ddagger\text{P}\text{IP}^{\circ}\text{PSPSC}\ddagger\text{P}$
 $\text{P}\pm\text{C}\ddagger\text{P}\rangle\text{P}\ddot{\text{e}}\ \text{PrPsPrP}^{\circ}\text{C},\text{PePsPIC}-\ \text{P}\ddot{\text{I}}\text{PsPIC}-\text{PrPsPjP}\rangle\text{P}_{\mu}\text{PSPSC}\ddagger\text{P}\ \text{P}\ddot{\text{C}}\ddagger\text{Ps}\ \text{PIP}\ddot{\text{e}}\text{P}\ddot{\text{I}}\text{P}^{\circ}\text{PrPeP}\ddot{\text{e}}$
 $\text{C},,\text{C}-\text{P}\pm\text{C}\ddagger\text{P}\ddot{\text{e}}\text{P}\rangle\text{C}\ddagger\text{C}\ddagger\text{C}-\text{C}-\ \text{P}\ddot{\text{I}}\text{P}_{\mu}\text{C}\ddagger\text{P}_{\mu}\text{PrC}\ddagger\text{P}_{\mu}\text{C}\ddagger\text{PrCH},\ \text{P}^{\circ}\text{C}\ddagger\text{P}\ddot{\text{e}}\text{C},\text{PjC}-\text{C}-,$
 $\text{C},\text{P}^{\circ}\text{C}...\text{C}-\text{PeP}^{\circ}\text{C}\ddagger\text{PrC}-\text{C}-,\ \text{PrP}\ddot{\text{e}}\text{C}\ddagger\text{P}\ddot{\text{I}}\text{PSPsP}_{\mu},\text{B}\ \text{PSPsC}\ddagger\text{PsPIP}\ddot{\text{e}}\text{C}...\ \text{PeC}\ddagger\text{PsPIP}\text{sC},\text{P}_{\mu}\text{C}\ddagger,$
 $\text{P}\ddot{\text{I}}\text{PsC}\ddagger\text{C}\ddagger\text{C}\ddagger\text{P}_{\mu}\text{PSC}\ddot{\text{H}}\ \text{P}\cdot\text{PsC}\ddagger\text{C}\ddagger,\ \text{P}\ \text{C},.\ \text{C}\ddagger.\ \text{C}\ddagger\ \text{PIP}\ddot{\text{e}}\text{P}\ddot{\text{I}}\text{P}\rangle\text{C}\ddagger\text{PrC}-\ \text{P}\cdot\text{PSP}\ddot{\text{e}}\text{P}\ddot{\text{I}}\text{P}_{\mu}\text{PSPSC}\ddagger\text{P}\ \text{P}_{\mu}\text{PsPiPs}$
 $\text{PiPsC}\ddagger\text{C},\text{C}\ddagger\text{PsC},\text{P}\ddot{\text{e}},\ \text{PjC}\ddagger\text{P}\rangle\text{CH}\text{C},\text{P}\ddot{\text{e}}\text{C},,\text{PsC}\ddagger\text{PjPSP}\text{sC}-\ \text{P}_{\mu}\text{C}\ddagger\text{P}\ddot{\text{e}}\text{C},\text{P}_{\mu}\text{PjP}\ddot{\text{e}},$
 $\text{P}_{\mu}\text{PeC}\ddagger\text{C},,\text{PsP}\rangle\text{C}-\text{P}^{\circ}\text{C},\text{P}\ddot{\text{e}}\text{PIPSPsPiPs}\ \text{PrP}_{\mu}\text{C}\ddagger\text{PjP}^{\circ}\text{C},\text{P}\ddot{\text{e}}\text{C},\text{C}\ddagger\ \text{C},\text{P}^{\circ}\ \text{C}\ddagger\text{C}\ddagger\text{C}...\text{PsC}\ddagger\text{C},\text{C}-$
 $\text{C}\ddagger\text{P}\rangle\text{P}\ddot{\text{e}}\text{P}\cdot\text{PsPIP}\text{sC}-\ \text{PsP}\pm\text{PsP}\rangle\text{PsPSPeP}\ddot{\text{e}}\ \text{C}\ddagger\text{PsC},\text{PsPIP}\text{sC}-\ \text{P}\ddot{\text{I}}\text{PsC}\ddagger\text{PsP}\ddot{\text{I}}\text{PSP}\ddot{\text{e}}\text{PSP}\ddot{\text{e}},$
 $\text{P}^{\circ}\text{C}\ddagger\text{PsC}\ddagger\text{C}-\text{P}_{\mu}\text{PsPIP}^{\circ}\text{PSC}-\ \text{C}-\text{P}\cdot\ \text{P}\cdot\text{P}^{\circ}\text{C}\ddagger\text{C},\text{PsC}\ddagger\text{C}\ddagger\text{P}\text{IP}^{\circ}\text{PSPSC}\ddagger\text{Pj}\ \text{C},\text{P}^{\circ}\text{PjC}\ddagger\text{C}\ddagger\text{P}\rangle\text{PsP}\cdot\text{P}\ddot{\text{e}}\text{PSC}\ddagger.$

P†PSC€C- P†P°PSC-

PJ C...PsPrC- PeP»C-PSC-C†PSPsPiPs PrPsC†P»C-PrP¶PµPSPSC¶ (PrPsC†P»C-PrP¶PµPSPSC¶ REDUCE) Cr C†PsP»PsPIC-PeC-PI, C¶PeC- P»C-PeC†PIP°P»PëC†C¶ PrC†C,P°C†C,PµC¶PëPrPsPj, PIC-PrP·PSP°C†P°P»P°C†C¶ PIPëC%oP° C†P°C†C,PsC,P° PIPëPSPëPePSPµPSPSC¶ C¶P°PeCr PiPµC¶PµPrPjC-C...CrC¶PsPIPsC— P·P°P»PsP·PëB (P·P° C€PeP°P»PsC¶ P“P»C-C†PsPSP° B¶“ 8B¶“10) PiPsC¶C-PIPSC¶PSPs P· PiC¶C†PiPsC¶ PiP»P°C†PµP±Ps (PrPëPI. C¶PsP·PrC-P»Pë B«PhC†PsP±P»PëPIPsC†C,C- P·P°C†C,PsC†C†PIP°PSPSC¶B» C,P° B«PαP°C¶PjP°PePsP»PsPiC-C†PSC- PIP»P°C†C,PëPIPsC†C,C-B»). PµC¶PëC†PëPSPSPsPiPs P·PiB¶™ C¶P·PeCr PjC-P¶ P·P°C†C,PsC†C†PIP°PSPSC¶Pj PrC†C,P°C†C,PµC¶PëPrC†C,P° PIPëPSPëPePSPµPSPSC¶Pj C¶P°PeCr PiPµC¶PµPrPjC-C...CrC¶PsPIPsC— P·P°P»PsP·Pë PIPëC†PsPePsC— PiC¶P°PrP°C†C-C— P·P° P“P»C-C†PsPSPsPj PIC†C,P°PSPsPIP»PµPSPs PSPµ P±C†P»Ps.

$P - P^\circ \text{ Pr}^\circ \text{PSP} \ddot{\text{P}} \text{P} \ddot{\text{P}} \text{PeP} \gg C - \text{PSC} - C \ddagger \text{PSP} \ddot{\text{P}} \text{C} \dots \text{PrPsC} \dot{\text{I}} \text{P} \gg C - \text{PrP} \parallel \text{P} \mu \text{PSC} \text{H} \text{C}, P^\circ$
 $\text{PiPsC} \dot{\text{I}} \text{C}, \text{PjP}^\circ \text{C} \ddot{\text{H}} \text{PeP} \mu \text{C}, \text{P} \ddot{\text{P}} \text{SPiPsPIP} \ddot{\text{P}} \text{C} \dots \text{C} \dot{\text{I}} \text{PiPsC} \dot{\text{I}} \text{C}, \text{P} \mu \text{C} \ddot{\text{H}} \text{P} \mu \text{P} \parallel \text{P} \mu \text{PSC} \text{H} \text{P} \pm \text{C} \dot{\text{r}} \text{P} \gg \ddot{\text{P}} \text{e}$
 $\text{PiPsPIC} - \text{PrPsPjP} \gg \text{P} \mu \text{PSPSC} \sqcup \text{PiC} \ddot{\text{H}} \text{Ps} \text{PIP} \ddot{\text{P}} \text{Pi}^\circ \text{PrPeP} \ddot{\text{P}} \text{C} \ddot{\text{H}} \text{P}^\circ \text{PeC} \dot{\text{r}} \text{PiC} \ddot{\text{H}} \text{C} \dot{\text{r}} \text{PrPSP} \text{C} - \text{P} \cdot \text{P}^\circ \text{P} \gg \text{PsP} \cdot \text{P} \ddot{\text{P}} \text{C} \dot{\text{r}}$
 $C \ddagger \text{PsP} \gg \text{PsPIC} - \text{PeC} - \text{PI} (\text{PrP} \ddot{\text{P}} \text{PI}, \text{C} \ddot{\text{H}} \text{PsP} \cdot \text{PrC} - \text{P} \gg \text{B} \ll \text{PhC} \dot{\text{I}} \text{PsP} \pm \text{P} \gg \text{P} \ddot{\text{P}} \text{PIPsC} \dot{\text{I}} \text{C}, C -$
 $\text{P} \cdot \text{P}^\circ \text{C} \dot{\text{I}} \text{C}, \text{PsC} \dot{\text{I}} \text{C} \dot{\text{r}} \text{PIP}^\circ \text{PSPSC} \sqcup \text{B} \gg).$

PŷPμCḡPjC-PS PïCḡPëPṛP°C,PSPsCĠC,C-.

2 C₇H₉PsPεPë.

PJPjPsPIPë P·P±PμCḡC-PiP°PSPSCİİ.

P—P±PμCḡC-PiP°C,Pë PïCḡPë C,PμPjPïPμCḡP°C,CrCḡC- PSPμ PIPëC‰Pμ 25 B°PŸ.

P—P±PμCḡC-PiP°C,Pë Cr PSPμPrPsCfC,CrPïPSPsPjCr PrP»Cİİ PrC-C,PμPNë PjC-CfC†C-.

PJPïP°PePsPIPeP°.

PkPμPïCḡPsP·PsCḡC- C„P»P°PePsPSPë P· PïPsP»C-PμC,PëP»PμPSCr PIPëCfPsPePsC—
C‰C-P»CHbPSPsCfC,C- P±C-P»PsPiPs PePsP»CHbPsCḡCr P·
PïPsP»C-PïCḡPsPïC-P»PμPSPsPIPëPjPë PeCḡPëC€PeP°PjPë, C‰Ps PjP°CḡC,CHb P·P°C...PëCfC,
PIC-Pr PIC-PrPeCḡPëC,C,Cİİ PrC-C,CHbPjPë, PïPs 30 P°P±Ps PïPs 90 PeP°PïCfCrP» Cr
C„P»P°PePsPSC-; PïPs 1 C„P»P°PePsPSCr PI PeP°CḡC,PsPSPSC-PNë PePsCḡPsP±C†C-.

PḡP°C,PμPiPsCḡC-Cİİ PIC-PrPïCrCfPeCr. P—P° CḡPμC†PμPïC,PsPj.

P’PëCḡPsP±PSPëPe.

PḡP°C,P°P»PμPSC, P”P¶PμCḡPjPμPSC- PëPsCḡPSPrPsCḡC„ P”PjP±Pİ, PkC-PjPμC†C†PëPSP°/

Catalent Germany Schorndorf GmbH, Germany.

**PḡC-CfC†PμP·PSP°C...PsPrP¶PμPSPSCİİ PIPëCḡPsP±PSPëPeP° C,P° PNëPsPiPs
P°PrCḡPμCfP° PjC-CfC†Cİİ PïCḡPsPIP°PrP¶PμPSPSCİİ PrC-CİİP»CHbPSPsCfC,C-.**

PëC,P°PNëPSP±P°PNëC€C,CḡP°CfCfPμ 1 C- 2, PëPsCḡPSPrPsCḡC„, P’P°PrPμPS-
P’CrCḡC,PμPjP±PμCḡPi, 73614, PkC-PjPμC†C†PëPSP°/

Steinbeisstr. 1 und 2, Schorndorf, Baden-Wuerttemberg, 73614, Germany.