

Р†РќРЎРЎР РЈРЉРІР†РІ

**РrР»CЦ РjРµРrРёC±PSPsPiPs Р·Р°CГC,PsCГCГPIР°PSPSCЦ Р»C-РeР°CГCГЧРePsPiPs
Р·Р°CГPs±CГ**

ОРЉР>РћРЎ^{В®}

(OMLOS^{В®})

РЎРeР»Р°Рr:

РrC-CHC±Р° CГРµC±PsPIРёPSP°: C,Р°РјCГCГР»PsР·РёPSCГ PiC-РrCГPsC...Р»PsCГРёРr;

1 РeР°РiCГCГР»Р° РjC-CГC,РёC,CH 0,4 РjPi C,Р°РјCГCГР»PsР·РёPSCГ
PiC-РrCГPsC...Р»PsCГРёРrCГ;

РrPsPiPsРjC-Р¶PSC- CГРµC±PsPIРёPSPё:

*PIРjiCГC, РeР°РiCГCзР»Рё: C†РµР»»CHР»PsР·Р° РjC-РeCГPsРeCГРёCГC,Р°Р»C-C±PSP°,
РjРµC,Р°РeCГРёР»Р°C,PSPsPiPs CГPsPiPsР»C-РjРµCГCГ РrРёCГPiРµCГCГC-CЦ,
PiPsР»C-CГPsCГР±Р°C, 80, PSP°C,CГC-CГ Р»Р°CГCГРёР»CГCГР»CHC,,Р°C,,
C,CГРёРµC,РёР»C†РёC,CГР°C,, C,Р°Р»CHРe;*

*PsР±PsР»PsPSPeР° РeР°РiCГCзР»Рё: Р¶РµР»»Р°C,РёPS, C-PSPrРёPiPsРeР°CГРjC-PS FD&C
CГРёPSC-Р№ 2 (Р• 132), C,РёC,Р°PSCГ РrC-PsРeCГРёРr (Р• 171), Р·Р°Р»C-Р·Р° PsРeCГРёРr
C±PsCГPSPёР№ (Р• 172), Р·Р°Р»C-Р·Р° PsРeCГРёРr C±РµCГPIPsPSPёР№ (Р• 172), Р·Р°Р»C-Р·Р°
PsРeCГРёРr Р¶PsPIC,РёР№ (Р• 172).*

**Р»C-РeР°CГCГЧРeР° C,,PsCГРjР°. РљР°РiCГCГР»Рё Р· РjPsРrРёC,,C-РePsPIР°PSPёРj
PIРёPIC-Р»CHPSPµPSPSCЦРj, C,PIРµCГРrC-.**

*РћCГPSPsPIРSC- C,,C-Р·РёРePs-C...C-РjC-C±PSC- PIР»Р°CГC,РёPIPsCГC,C-: C,PIРµCГРi
Р¶РµР»»Р°C,РёPSPsPi РeР°РiCГCГР»Рё Р· РePsCГРiCГCГPsРj PiPsРjР°CГР°PSC±РµPIPsPiPs
РePsР»CHPsCГCГ C,Р° РeCГРёCёРePsCГ PsР»РёPIРePsPIPsPiPs РePsР»CHPsCГCГ. Р'РjiCГC,
РeР°РiCГCГР» – PiCГР°PSCГР»Рё PiРr Р±iР»PsPiPs РrPs РjР°Р№Р¶Рµ Р±iР»PsPiPs
РePsР»CHPsCГCГ.*

**Р°Р°CГРjР°РePsC,РµCГР°РiРµPIC,РёC±PSP° РiCГCГРiР°. Р—Р°CГPsР±Рё, C%Ps
Р·Р°CГC,PsCГPsPICГCHC,CHCГCЦ PiCГРё РrPsР±CГPsCЦРeC-CГPSC-Р№
PiC-PiРµCГРiР»Р°C-C— PiРµCГРµРjC-C...CГCГPsPIPsC— Р·Р°Р»PsР·Рё.
РћPSC,Р°PiPsPSC-CГC,Рё α₁-Р°РrCГРµPSPµCГPiC-C±PSPёC... CГРµC†РµPiC,PsCГC-PI.B РљPsРr
РћРЎРІ G04C A02.**

PαP°CḡPjP°PePsP»PsPiC-C‡PSC- PIP»P°CḡC,PëPIPsCḡC,C-.

PαP°CḡPjP°PePsPrPëPSP°PjC-PeP°.

PŷP°PjCḡCḡP»PsP·PëPS PIPëP±C-CḡPePsPIPs C- PePsPSPeCḡCḡPμPSC,PSPs P±P»PsPeCḡC”
PİPsCḡC,CḡPëPSP°PiC,PëC‡PSC- α₁-P°PrCḡPμPSPsCḡPμC†PμPiC,PsCḡPë, P·PsPeCḡPμPjP° α_{1A}
C,P° α_{1D}, C%oPs P·PSP°C...PsPrCḡC,CḡCḡCḡ Cḡ PiP»P°PrPμPSCḡPeC-PNë
PjCḡCḡPeCḡP»P°C,CḡCḡC- PİPμCḡPμPrPjC-C...CḡCḡPsPIPsC— P·P°P»PsP·Pë, CëPëPNëPePë
CḡPμC‡PsPIPsPiPs PjC-C...CḡCḡP° C- PİCḡPsCḡC,P°C,PëC‡PSPsC— C‡P°CḡC,PëPSPë
CḡCḡPμC,CḡPë. PİPμ PİCḡPëP·PIPsPrPëC,Ch PrPs P·PSPëP¶PμPSPSCḡ C,PsPSCḡCḡCḡ
PiP»P°PrPμPSCḡPePsC— PjCḡCḡPeCḡP»P°C,CḡCḡPë PİPμCḡPμPrPjC-C...CḡCḡPsPIPsC—
P·P°P»PsP·Pë, CëPëPNëPePë CḡPμC‡PsPIPsPiPs PjC-C...CḡCḡP° C- PİCḡPsCḡC,P°C,PëC‡PSPsC—
C‡P°CḡC,PëPSPë CḡCḡPμC,CḡPë C,P° PİPsP»C-PİCëPμPSPSCḡ PIPëPrC-P»PμPSPSCḡ CḡPμC‡C-.
PhPrPSPsC‡P°CḡPSPs P·PjPμPSCëCḡCḡC,CḡCḡCḡ CḡPëPjPİC,PsPjPë PsP±CḡC,CḡCḡPeC†C-C—
C,P° PİPsPrCḡP°P·PSPμPSPSCḡ, PİPsPIBḡ™ CḡP·P°PSC- P· PrPsP±CḡPsCḡPeC-CḡPSPsCḡ
PiC-PİPμCḡPİP»P°P·C-C”Cḡ PİPμCḡPμPrPjC-C...CḡCḡPsPIPsC— P·P°P»PsP·Pë
(CḡC,CḡCḡPrPSPμPSPSCḡ PİPsC‡P°C,PeCḡ CḡPμC‡PsPIPëPİCḡCḡPeP°PSPSCḡ,
PİPsCḡP»P°P±P»PμPSPSCḡ CḡC,CḡCḡPjPμPSCḡ CḡPμC‡C-, PeCḡP°PİP°PSPSCḡ PİC-CḡP»Cḡ
P·P°PeC-PSC‡PμPSPSCḡ CḡPμC‡PsPIPëPİCḡCḡPeP°PSPSCḡ, PIC-PrC‡CḡC,C,Cḡ
PSPμPİPsPIPsPiPs CḡPİPsCḡPsP¶PSPμPSPSCḡ CḡPμC‡PsPIPsPiPs PjC-C...CḡCḡP°, C‡P°CḡC,C-
PİPsP·PëPIPë PrPs CḡPμC‡PsPIPëPİCḡCḡPeP°PSPSCḡ, PİPsP·PëPIPë PrPs
CḡPμC‡PsPIPëPİCḡCḡPeP°PSPSCḡ PI PSC-C‡PSPëPNë C‡P°Cḡ, PSPμPIC-PrPeP»P°PrPSC-CḡC,Ch
CḡPμC‡PsPIPëPİCḡCḡPeP°PSPSCḡ).

PİC- PμC,,PμPeC,Pë PrPsPIPiPëPNë C‡P°Cḡ P·P±PμCḡC-PİP°CḡC,CḡCḡCḡ PİCḡPë
PrPsPIPiPsCḡC,CḡPsPePsPIPsPjCḡ P»C-PeCḡPIP°PSPSC- C- P·PSP°C‡PSPsCḡ PjC-CḡPsCḡ
CḡC,CḡPëPjCḡCḡC,Ch PİCḡPsPIPμPrPμPSPSCḡ C...C-CḡCḡCḡPiC-C‡PSPsC—
PsPİPμCḡP°C†C-C— P°P±Ps PeP°C,PμC,PμCḡPëP·P°C†C-C—.

PhPSC,P°PiPsPSC-CḡC,Pë α₁-P°PrCḡPμPSPsCḡPμC†PμPiC,PsCḡC-PI PjP°CḡC,Ch
P·PrP°C,PSC-CḡC,Ch P·PSPëP¶CḡPIP°C,Pë P°CḡC,PμCḡC-P°P»ChPSPëPNë C,PëCḡPe
CëP»CḡC...PsPj P·PSPëP¶PμPSPSCḡ PİPμCḡPëC,,PμCḡPëC‡PSPsPiPs C,PsPSCḡCḡCḡ CḡCḡPrPëPS.
PμC-Pr C‡P°Cḡ PİCḡPsPIPμPrPμPSPSCḡ PIPëPİCḡPsP±CḡPIP°PSCḡ C,P°PjCḡCḡP»PsP·PëPSCḡ
PSPμ PIC-PrP·PSP°C‡P°P»PsCḡCḡ PeP»C-PSC-C‡PSPs PIPëCḡP°P¶PμPSPsPiPs
P·PSPëP¶PμPSPSCḡ P°CḡC,PμCḡC-P°P»ChPSPsPiPs C,PëCḡPeCḡ.

PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°.

P’CḡPjPsPeC,CḡPIP°PSPSCḡ

PŷP°PjCḡCḡP»PsP·PëPS PrPsP±CḡPμ PICḡPjPsPeC,CḡC”C,CḡCḡCḡ P·i CëP»CḡPSPePsPIPsPiPs-
PePëCëPePsPIPsPiPs C,CḡP°PeC,Cḡ, P° PNëPsPiPs P±C-PsPrPsCḡC,CḡPİPSC-CḡC,Ch
CḡC,P°PSPsPIPëC,Ch PjP°PNëP¶Pμ 100 %. P’CḡPjPsPeC,CḡPIP°PSPSCḡ C,P°PjCḡCḡP»PsP·PëPSCḡ
PIC-PrP±CḡPIP°C”C,CḡCḡCḡ PrPμC%oPs PİPsPIC-P»ChPSC-CëPμ PİC-CḡP»Cḡ
PIP¶PëPIP°PSPSCḡ C—P¶C-. PhPrPSPsCḡC-PrPSC-CḡC,Ch PICḡPjPsPeC,CḡPIP°PSPSCḡ
PrPsCḡCḡPİP°C”C,CḡCḡCḡ PI C,PsPjCḡ PIPëPİP°PrPeCḡ, PePsP»Pë PİP°C†C-C”PSC,
PİCḡPëPNëPjP°C” C,P°PjCḡCḡP»PsP·PëPS, PeP°PİCḡCḡP»Pë P· PjPsPrPëC,,C-PePsPIP°PSPëPj
PIPëPIC-P»ChPSPμPSPSCḡPj, PI PsPrPëPS C- C,PsPNë CḡP°PjPëPNë C‡P°Cḡ PİC-CḡP»Cḡ
PIP¶PëPIP°PSPSCḡ C—P¶C-. PαP°CḡPjP°PePsPeC-PSPμC,PëPeP° C,P°PjCḡCḡP»PsP·PëPSCḡ PjP°C”
P»C-PSC-PNëPSPëPNë C...P°CḡP°PeC,PμCḡ.

PμC-CḡP»Cḡ PİCḡPëPNëPsPjCḡ CḡP°P·PsPIPsC— PrPsP·Pë C,P°PjCḡCḡP»PsP·PëPSCḡ,

PeP°PiCfCfP»Pë P· PjPsPrPëC,,C-PePsPIP°PSPëPj PIPëPIC-P»CHbPSPµPSPSCfPj, Pïc-CfP»Cf PIP¶PëPIP°PSPSCf C—P¶C- PjP°PeCfPëPjP°P»CHbPSP° PePsPSC†PµPSC,CfP°C†C-Cf B (C_{max}) C,P°PjCfCfP»PsP·PëPSCf Cf PïP»P°P·PjC- PeCfjPsPIC- PrPsCfCfPïP°C”C,CHbCfCf PïcCfPëP±P»PëP·PSPs C†PµCfjPµP· 6 PiPsPrPëPS, P° CfC,P°P±C-P»CHbPSP° PePsPSC†PµPSC,CfP°C†C-Cf CfC,PIPsCfjCfC”C,CHbCfCf PSP° Pïb[™] CfC,Cf PrPsP±Cf Pïc-CfP»Cf C°PsPrPµPSPSPsPiPs PïcCfPëPNëPsPjCf PïcCfPµPïP°CfP°C,Cf. C_{max} PïcCfPë C†CHbPsPjCf C” PïcCfPëP±P»PëP·PSPs PSP° PrPIC- C,CfjPµC,PëPSPë PIPëC°PsCf P·P° C,Cf, C°Ps CfC,PIPsCfjCfC”C,CHbCfCf Pïc-CfP»Cf PïcCfPëPNëPsPjCf CfP°P·PsIPsC— PrPsP·Pë.

P PsP·PïPsPrC-P»

Pj C†PsP»PsPIC-PeC-PI C,P°PjCfCfP»PsP·PëPS PïcCfPëP±P»PëP·PSPs PSP° 99 % P·PiB[™] CfC·CfC”C,CHbCfCf P· P±C-P»PeP°PjPë PïP»P°P·PjPë PeCfjPsPIC-. PhP±B[™] C”Pj CfjPsP·PïPsPrC-P»Cf PïcCfPµPïP°CfP°C,Cf PSPµP·PSP°C†PSPëPNë (PïcCfPëP±P»PëP·PSPs 0,2 P»/PePi).

PµPµC,P°P±PsP»C-P·Pj

PÿP°PjCfCfP»PsP·PëPSCf Pïc-PrCfjPsC...P»PsCfjPëPr PSPµ Pïc-PrPrP°C”C,CHbCfCf PµC,,PµPeC,Cf PïPµCfjCëPsPiPs PïcCfjPsC...PsPrP¶PµPSPSCf C- PïPsPIC-P»CHbPSPs PjPµC,P°P±PsP»C-P·CfC”C,CHbCfCf Cf PïPµC†C-PSC†C- P· CfC,PIPsCfjPµPSPSCfPj C,,P°CfjPjP°PePsP»PsPïc-C†PSPs P°PeC,PëPIPSPëC... PjPµC,P°P±PsP»C-C,PI, C°Ps P·P±PµCfC-PïP°CfC,CHb PIPëCfPsPeCf CfPµP»PµPeC,PëPIPSC-CfC,CHb PrPs α₁- P°PrCfjPµPSPsCfjPµC†PµPïc,PsCfjC-PI. P’C-P»CHbCëP° C†P°CfC,PëPSP° P°PeC,PëPIPSPsC— CfjPµC†PsPIPëPSPë PSP°CfPIPSP° PI PeCfjPsPIC- Cf PSPµP·PjC-PSPµPSPsPjCf PIPëPiP»CfPrC-.

P·P»C-PjC-PSP°C†C-Cf

PÿP°PjCfCfP»PsP·PëPS C,P° PNëPsPiPs PjPµC,P°P±PsP»C-C,Pë PIPëPIPsPrCfC,CHbCfCf P· PsCfjPïP°PSC-P·PjCf PïPµCfjPµPIP°P¶PSPs C-P· CfPµC†PµCf. PµCfjPëP±P»PëP·PSPs 9 % PIC-Pr PrPsP·Pë P·P°P»PëCëP°C”C,CHbCfCf Cf PIPëPiP»CfPrC- PSPµP·PjC-PSPµPSPsC— PrC-CfC†PsC— CfjPµC†PsPIPëPSPë.

PµC-CfP»Cf CfP°P·PsIPsPiPs PïcCfPëPNëPsPjCf PrPsP·Pë C,P°PjCfCfP»PsP·PëPSCf, PeP°PiCfCfP»Pë P· PjPsPrPëC,,C-PePsPIP°PSPëPj PIPëPIC-P»CHbPSPµPSPSCfPj, Pïc-CfP»Cf PIP¶PëPIP°PSPSCf C—P¶C- C,P° PïcCfPë CfC,P°P±C-P»CHbPSC-PNë PePsPSC†PµPSC,CfP°C†C-C— Cf PïP»P°P·PjC- PeCfjPsPIC- PïPµCfjC-PsPr PSP°Pïc-PIPIPëPµPrPµPSPSCf PIC-PrPiPsPIC-PrPSPs CfC,P°PSPsPIPëC,CHb PïcCfPëP±P»PëP·PSPs 10 C,P° 13 PiPsPrPëPS.

PµP»C-PSC-C†PSC- C...P°CfjP°PeC,PµCfjPëCfC,PëPePë.

PµPsPeP°P·P°PSPSCf.

P>C-PeCfPIP°PSPSCf C,,CfPSPeC†C-PsPSP°P»CHbPSPëC... CfjPsP·P»P°PrC-PI P· P±PsPeCf PSPëP¶PSC-C... CfPµC†PsPIPëC... CëP»CfC...C-PI PïcCfPë PrPsP±CfjPsCfPeC-CfPSC-PNë Pïc-PïPµCfjPïP»P°P·C-C— PïcCfjPsCfC,P°C,Pë.

PµCfjPsC,PëPïPsPeP°P·P°PSPSCf.

P“C-PiPμC7C4CfC,P»PëPIC-CfC,CH PrPs C,P°PjCfCfP»PsP·PëPSCf
 PiC-PrC7PsC...P»PsC7PëPrCf, PIPeP»C7C4P°C7C4Pë PjPμPrPëPeP°PjPμPSC,PsP·PSPs-
 C-PSPrCfPePsPIP°PSPëPNë P°PSPiC-PsPSPμPIC7PsC,PëC4PSPëPNë PSP°P±C7C4IPe, P°P±Ps PrPs
 P±CfPrCH-C4IPePsC— P· PrPsPiPsPjC-P7PSPëC... C7PμC4PsPIPëPS P»C-PeP°C7CfCHPePsPiPs
 P·P°CfPsP±Cf; PSP°C4PIIPSC-CfC,CH PI P°PSP°PjPSPμP·C- PsC7C,PsCfC,P°C,PëC4PSPsC—
 PiC-PiPsC,PμPSP·C-C—; C,C4P7PeP° PiPμC4C-PSPePsPIP° PSpμPrPsCfC,P°C,PSC-CfC,CH.

**P'P·P°C"PjPsPrC-C4 P· C-PSCëPëPjPë P»C-PeP°C7CfCHPePëPjPë P·P°CfPsP±P°PjPë C,P°
 C-PSCëC- PIPëPrPë PIP·P°C"PjPsPrC-PNë.**

P"PsCfP»C-PrP7PμPSPSC4 PIP·P°C"PjPsPrC-C— PIPëPePsPSCfPIP°P»PëCfCH C,C-P»CHPePë Cf
 PrPsC7PsCfP»PëC....

P4C7Pë PsPrPSPsC4P°CfPSPsPjCf P·P°CfC,PsCfCfPIP°PSPSC- C,P°PjCfCfP»PsP·PëPSCf
 PiC-PrC7PsC...P»PsC7PëPrCf P· P°C,PμPSPsP»PsP»PsPj, PμPSP°P»P°PiC7PëP»PsPj,
 PSC-C,,PμPrPëPiC-PSPsPj P°P±Ps C,PμPsC,,C-P»C-PSPsPj P»C-PeP°C7CfCHPePsC—
 PIP·P°C"PjPsPrC-C— PSPμ PIC-PrP·PSP°C4P°P»PsCfC4.

PhPrPSPsC4P°CfPSPμ P·P°CfC,PsCfCfPIP°PSPSC4 P· C4PëPjPμC,PëPrPëPSPsPj
 PiC-PrPIPëC%oCfC", P° P· C,,CfC7PsCfPμPjC-PrPsPj — P·PSPëP7CfC"
 PePsPSC4PμPSC,C7P°C4C-CH C,P°PjCfCfP»PsP·PëPSCf Cf PiP»P°P·PjC- PeC7PsPIC-, P°P»Pμ
 PsCfPeC-P»CHPePë C4C- C7C-PIPSC- P·P°P»PëCëP°C7C,CHCfC4 Cf PjPμP7P°C... PSPsC7PjPë,
 Cf CfPiPμC4C-P°P»CHPSC-PNë PePsC7PμPeC4C-C— PrPsP·CfPIP°PSPSC4
 C,P°PjCfCfP»PsP·PëPSCf PSPμPjP°C" PiPsC,C7PμP±Pë.

Pj PrPsCfP»C-PrP7PμPSPSC4C... *in vitro* PrC-P°P·PμPiP°Pj, PiC7PsPiC7P°PSPsP»PsP»,
 C,C7PëC...P»PsC7PjPμC,C-P°P·PëPr, C...P»PsC7PjP°PrPëPSPsPS, P°PjC-C,C7PëPiC,PëP»C-PS,
 PrPëPeP»PsC,,PμPSP°Pe, PiP»C-P±PμPSPeP»P°PjC-Pr, CfPëPjPIP°CfC,P°C,PëPS C,P°
 PIP°C7C,,P°C7PëPS PSPμ PIPiP»PëPIP°C7C,CH PSP° PIC-P»CHPSCf C,,C7P°PeC4C-CH
 C,P°PjCfCfP»PsP·PëPSCf Cf PiP»P°P·PjC- PeC7PsPIC- P»CHPrPëPSPë. P4PsPrC-P±PSPëPj
 C4PëPSPsPj C,P°PjCfCfP»PsP·PëPS PSPμ P·PjC-PSCH" C7C-PIPμPSC7 PIC-P»CHPSPëC...
 C,,C7P°PeC4C-PNë PrC-P°P·PμPiP°PjCf, PiC7PsPiC7P°PSPsP»PsP»Cf,
 C,C7PëC...P»PsC7PjPμC,C-P°P·PëPrCf C,P° C...P»PsC7PjP°PrPëPSPsPSCf Cf PiP»P°P·PjC-
 PeC7PsPIC- P»CHPrPëPSPë.

P4C7PsC,Pμ PrPëPeP»PsC,,PμPSP°Pe C,P° PIP°C7C,,P°C7PëPS PjPsP7CfC,CH
 PiC-PrPIPëC%oCfPIP°C,Pë CëPIPëPrPeC-CfC,CH PμP»C-PjC-PSP°C4C-C—
 C,P°PjCfCfP»PsP·PëPSCf.

PhPrPSPsC4P°CfPSPμ P·P°CfC,PsCfCfPIP°PSPSC4 C,P°PjCfCfP»PsP·PëPSCf
 PiC-PrC7PsC...P»PsC7PëPrCf P· CfPëP»CHPSPëPjPë C-PSPiC-P±C-C,PsC7P°PjPë CYP3A4
 PjPsP7Pμ PiC7PëP·PIPμCfC,Pë PrPs P·P±C-P»CHCëPμPSPSC4 PIPiP»PëPICf
 C,P°PjCfCfP»PsP·PëPSCf PiC-PrC7PsC...P»PsC7PëPrCf. PhPrPSPsC4P°CfPSPμ
 P·P°CfC,PsCfCfPIP°PSPSC4 P· PePμC,PsPePsPSP°P·PsP»PsPj (PIC-PrPsPjPëPNë
 CfPëP»CHPSPëPNë C-PSPiC-P±C-C,PsC7 CYP3A4) PiC7PëP·PIPsPrPëP»Ps PrPs
 P·P±C-P»CHCëPμPSPSC4 PiP»PsC%oC- PiC-Pr C,,P°C7PjP°PePsPeC-PSPμC,PëC4PSPsC7
 PeC7PëPIPsC7 B«PePsPSC4PμPSC,C7P°C4C-C4P°CfB» (AUC) C- PŸ_{max} PrPs 2,8 C- 2,2
 PIC-PrPiPsPIC-PrPSPs.

PŸP°PjCfCfP»PsP·PëPSCf PiC-PrC7PsC...P»PsC7PëPr PSPμ CfP»C-Pr PiC7PëP·PSP°C4P°C,Pë Cf

PePsPjP±C-PSP°C†C-C— P· CÍPëP»CHbPSPëPjPë C-PSPiC-P±C-C,PsCĤP°PjPë CYP3A4 CÍ
PİP°C†C-C”PSC,C-PI iP· PSPëP·CHbPePëPj PjPµC,P°P±PsP»C-P·PjPsPj CYP2D6.

PÿP°PjCÍCÍP»PsP·PëPSCÍ PiC-PrCĤPsC...P»PsCĤPëPr CÍP»C-Pr P· PsP±PµCĤPµP¶PSC-CÍC,CĤ
P·P°CÍC,PsCÍPsPICÍPIP°C,Pë CÍ PePsPjP±C-PSP°C†C-C— P· CÍPëP»CHbPSPëPjPë C-
PİPsPjC-CĤPSPëPjPë C-PSPiC-P±C-C,PsCĤP°PjPë CYP3A4.

PhPrPSPsC±P°CÍPSPµ P·P°CÍC,PsCÍCÍPIP°PSPSCİ C,P°PjCÍCÍP»PsP·PëPSCÍ
PiC-PrCĤPsC...P»PsCĤPëPrCÍ C- PİP°CĤPsPeCÍPµC,PëPSCÍ (CÍPëP»CHbPSPëPNë
C-PSPiC-P±C-C,PsCĤ PÿYP2D6) PİCĤPëP·PIPsPrPëC,CH PrPs P·P±C-P»CHbC€PµPSPSCİ Pÿ_{max} C-
AUC PrPs 1,3 C- 1,6 PIC-PrPİPsPIC-PrPSPs, P°P»Pµ C†Pµ PSPµ C” PeP»C-PSC-C±PSPs
P·PSP°C†CÍC%PëPj.

PhPrPSPsC±P°CÍPSPµ P·P°CÍC,PsCÍCÍPIP°PSPSCİ P· C-PSC€PëPjPë α₁-
P°PrCĤPµPSPsP±P»PsPeP°C,PsCĤP°PjPë PjPsP¶Pµ PİPsCÍPëP»CĤPIP°C,Pë
PiC-PİPsC,PµPSP·PëPIPSPëPNë PµC,,PµPeC,.

PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCıPIP°PSPSCİ.

PİPe C- PİCĤPë P·P°CÍC,PsCÍCÍPIP°PSPSC- C-PSC€PëC... α₁-
P°PrCĤPµPSPsP±P»PsPeP°C,PsCĤC-PI, PI PsPeCĤPµPjPëC... PİPëPİP°PrPeP°C... PİCĤPë
P·P°CÍC,PsCÍCÍPIP°PSPSC- C,P°PjCÍCÍP»PsP·PëPSCÍ PjPsP¶Pµ»PëPIPµ P·PSPëP¶PµPSPSCİ
P°CĤC,PµCĤC-P°P»CHbPSPsPiPs C,PëCÍPeCÍ, C%Ps PjPsP¶Pµ C-PSPsPrC- PİCĤPëP·PIPµCÍC,Pë
PrPs PIC,CĤP°C,Pë CÍPIC-PrPsPjPsCÍC,C-. PµCĤPë PİPsCİPIC- PİPµCĤC€PëC... PsP·PSP°Pe
PsCĤC,PsCÍC,P°C,PëC±PSPsC— PiC-PİPsC,PµPSP·C-C— (P·P°PİP°PjPsCĤPsC±PµPSPSCİ,
CÍP»P°P±PeC-CÍC,CH) PİP°C†C-C”PSC, PjP°C” PİCĤPëCÍC-CÍC,Pë C±Pë PİCĤPëPNëPSCİC,Pë
PİPsCĤPëP·PsPSC,P°P»CHbPSPµ PİPsP»PsP¶PµPSPSCİ PrPs P·PSPëPePSPµPSPSCİ
PIPëC%PµP·PİP°PrP°PSPëC... CÍPëPjPİC,PsPjC-PI.

PµPµCĤPµPr C,PëPj CİPe CĤPsP·PİPsC±P°C,Pë P»C-PeCÍPIP°PSPSCİ C,P°PjCÍCÍP»PsP·PëPSPsPj,
CÍP»C-Pr PİCĤPsPNëC,Pë PjPµPrPëC±PSPµ PsP±CÍC,PµP¶PµPSPSCİ P· PjPµC,PsCĤ
PIPëCİPIP»PµPSPSCİ C-PSC€PëC... CÍCÍPİCÍC,PSC-C... P·P°C...PIPsCĤCĤPIP°PSCĤ, C%Ps
PjPsP¶CÍC,CH CÍPİCĤPëC±PëPSPëC,Pë C,P°PeC- CÍP°PjC- CÍPëPjPİC,PsPjPë, CİPe
PrPsP±CĤPsCİPeC-CÍPSP° PiC-PİPµCĤPİP»P°P·C-Cİ PİPµCĤPµPrPjC-C...CÍCĤPsPIPsC—
P·P°P»PsP·Pë. PµPµCĤPµPr PİPsC±P°C,PePsPj P»C-PeCÍPIP°PSPSCİ PSPµPsP±C...C-PrPSPs
PİCĤPsPIPµCÍC,Pë CĤPµPeC,P°P»CHbPSPµ PsP±CÍC,PµP¶PµPSPSCİ
PİPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë C,P° PİCĤPë PSPµPsP±C...C-PrPSPsCÍC,C- -
C,PµCÍC, PSP° PİPëP·PSP°C±PµPSPSCİ CĤC-PIPSCİ CÍPİPµC†PëC,,C-C±PSPsPiPs
P°PSC,PëPİPµPSCÍ PİPµCĤPµPrPjC-C...CÍCĤPsPIPsC— P·P°P»PsP·Pë (PSA) PrPs PİPsC±P°C,PeCÍ
C,P° C±PµCĤPµP· PsPrPSP°PePsPIC- PİCĤPsPjC-P¶PePë C±P°CÍCÍ PİC-Pr C±P°CÍ
P»C-PeCÍPIP°PSPSCİ.

PµCĤPëP·PSP°C±P°C,Pë PİCĤPµPİP°CĤP°C, PİP°C†C-C”PSC,P°Pj C-P· C,CİP¶PePsCĤ
C,,PsCĤPjPsCĤ PSPëCĤPePsPIPsC— PSPµPrPsCÍC,P°C,PSPsCÍC,C- (PeP»C-CĤPµPSCÍ
PeCĤPµP°C,PëPSC-PSCÍ <10 PjP»/C...PI) PSPµPsP±C...C-PrPSPs P· PsCÍPsP±P»PëPIPsCĤ
PsP±PµCĤPµP¶PSC-CÍC,CĤ, PsCÍPeC-P»CHbPePë PeP»C-PSC-C±PSPëC...
PrPsCÍP»C-PrP¶PµPSCĤ C-P· P·P°CÍC,PsCÍCÍPIP°PSPSCİPj C,P°PjCÍCÍP»PsP·PëPSCÍ PrP»Cİ
C,P°PePëC... PİP°C†C-C”PSC,C-PI PSPµ PİCĤPsPIPsPrPëP»Pë.

PJ PrPµCİPePëC... PİP°C†C-C”PSC,C-PI, CİPeC- PİCĤPëPNëPjP°P»Pë P°P±Ps

$$P-P^{\circ}C\acute{I}C,PsC\acute{I}C\acute{z}PIP^{\circ}PSPSC\sqcup C\acute{z}P\ddot{I}P_{\mu}C\bar{H}C-PsPr PIP^{\circ}PiC-C,PSPsC\acute{I}C,C-P^{\circ}P\pm Ps$$

$$PiPsPrC\acute{z}PIP^{\circ}PSPSC\sqcup PiC\bar{H}C\acute{z}PrPrC\bar{H}.$$

*P'C-PrP·PSP°C±P°P»PëCÍCЦ Cr PíC-Cl'P»CЦCḡPμC"Cl'C,CḡP°C†C-PM̄PSPsPjCf
PīPμCḡC-PsPrC-.

PμC-Pr C±P°CÍ PíC-Cl'P»CЦCḡPμC"Cl'C,CḡP°C†C-PM̄PSPsPiPs PSP°PiP»CЦPrCf PsPīPëCÍP°PSC-
PIPëPīP°PrPePë C-PSC,CḡP°PsPīPμCḡP°C†C-PM̄PSPsC— PSPμCÍC,P°P±C-P»CH̄PSPsCÍC,C-
CḡP°PM̄PrCfP¶PSPsC— PsP±PsP»PsPSPePë PsPeP° (Cl'PëPSPPrCḡPsPj P·PICrP¶PμPSPsC—
P·C-PSPëC†C-) PíCḡPë PsPīPμCḡP°C†C-C— P· PíCḡPëPIPsPrCf PeP°C,P°CḡP°PeC,Pë C,P°
PiP»P°CfPePsPjPë Cr PīP°C†C-C"PSC,C-PI, CЦPeC- PíCḡPëPM̄PjP°P»Pë C,P°PjCÍCfP»PsP·PëPS
(PrPëPI. CḡPsP·PrC-P» B<PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCfPIP°PSPSCЦB»).

PμC-Cl'P»CЦCḡPμC"Cl'C,CḡP°C†C-PM̄PSPëPM̄ PrPsCÍPIC-Pr. PhPeCḡC-Pj
PIPëC%oPμPIPeP°P·P°PSPëC... PīPsP±C-C±PSPëC... CḡPμP°PeC†C-PM̄ P·P°C,,C-PeCÍPsPIP°PSPs
PIPëPīP°PrPePë C,,C-P±CḡPëP»CЦC†C-C— PīPμCḡPμPrCÍPμCḡPrCH̄, P°CḡPëC,PjC-C—,
C,P°C...C-PeP°CḡPrC-C— C,P° PrPëCÍPīPSPsPμ. PhCÍPeiP»CH̄PePë PíCḡPs P·P°P·PSP°C±PμPSC-
PIPëPīP°PrPePë PīPsPIC-PrPsPjP»CЦP»Pë Cl'PīPsPSC,P°PSPSPs, C±P°CÍC,PsC,P°
PīPsPIC-PrPsPjP»PμPSCḡ C,P° CḡPsP»CH̄ C,P°PjCÍCfP»PsP·PëPSCr Cr C†CH̄PsPjCf
PIPëPīP°PrPeCf PSPμ PjPsP¶CfC,CH̄ P±CfC,Pë PrPsCÍC,PsPIC-CḡPSPs
PICÍC,P°PSPsPIP»PμPSC-.

PμPsPIC-PrPsPjP»PμPSPSCЦ PíCḡPs PīPsP±C-C±PSC- CḡPμP°PeC†C-C— PíC-Cl'P»CЦ
CḡPμC"Cl'C,CḡP°C†C-C— P»C-PeP°CḡCÍCH̄PePsPiPs P·P°CÍPsP±Cf PjP°C" PIPμP»PëPePμ
P·PSP°C±PμPSPSCЦ. PīPμ PrP°C" P·PjPsPiCf PíCḡPsPIPsPrPëC,Pë PjPsPSC-C,PsCḡPëPSPi
Cl'PíC-PIPIC-PrPSPsC€PμPSPSCЦ PePsCḡPëCÍC,CH̄/CḡPëP·PëPe PíCḡPë
P·P°CÍC,PsCÍCfPIP°PSPSC- C†CH̄PsPiPs P»C-PeP°CḡCÍCH̄PePsPiPs P·P°CÍPsP±Cf.
Ph̄PμPrPëC±PSPëPj C,P° C,,P°CḡPjP°C†PμPIC,PëC±PSPëPj PíCḡP°C†C-PIPSPëPeP°Pj, P°
C,P°PePsP¶ PīP°C†C-C"PSC,P°Pj P°P±Ps C—C...PSC-Pj P·P°PePsPSPSPëPj
PíCḡPμPrCÍC,P°PIPSPëPeP°Pj Cl'P»C-Pr PīPsPIC-PrPsPjP»CЦC,Pë PíCḡPs CrCÍC-
PIPëPīP°PrPePë PíC-PrPsP·CḡCḡPIP°PSPëC... PīPsP±C-C±PSPëC... CḡPμP°PeC†C-PM̄ C,P°
PIC-PrCÍCfC,PSPsCÍC,C- PμC,,PμPeC,PëPIPSPsCÍC,C- P»C-PeP°CḡCÍCH̄PePsPiPs P·P°CÍPsP±Cf
C±PμCḡPμP· Ph̄PIC,PsPjP°C,PëP·PsPIP°PSCr C-PSC,,PsCḡPjP°C†C-PM̄PSCr Cl'PëCÍC,PμPjCf P·
C,,P°CḡPjP°PePsPSP°PiP»CЦPrCf P·P° PīPsCÍPëP»P°PSPSCЦPj: <http://aisf.dec.gov.ua>.

PḡPμCḡPjC-PS PíCḡPëPrP°C,PSPsCÍC,C-. 3 CḡPsPePë.

PkPμ P·P°CÍC,PsCÍPsPICrPIP°C,Pë PíC-Cl'P»CЦ P·P°PeC-PSC±PμPSPSCЦ C,PμCḡPjC-PSCr
PíCḡPëPrP°C,PSPsCÍC,C-, P·P°P·PSP°C±PμPSPsPiPs PSP° CrPīP°PePsPIC†C-.

PIPjPsPIPë P·P±PμCḡC-PiP°PSPSCЦ.

P"°PSPëPM̄ PíCḡPμPīP°CḡP°C, PSPμ PIPëPjP°PiP°C" PsCÍPsP±P»PëPIPsPiPs
C,PμPjPīPμCḡP°C,CrCḡPSPsPiPs CḡPμP¶PëPjCf P·P±PμCḡC-PiP°PSPSCЦ.

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

PJPİP°PePsPIPeP°.

PμPs 10 PeP°PiCfCfP» Cr P±P»iCfC,PμCḡi, PİPs 3 P±P»iCfC,PμCḡPë Cr PeP°CḡC,PsPSPSiPNë PePsCḡPsP±C†i.

PљP°C,PμPiPsCḡC-Cİİ PIC-PrPiCfCfPeCf.

P—P° CḡPμC†PμPiC,PsPj.

P’PëCḡPsP±PSPëPe.

PḡP>PљPḡP>PhP†P” PḡP” PŸPePsPİbḡ™C”.

ALKALOID AD Skopje.

PњC-CfC†PμP•PSP°C...PsPrP¶PμPSPSCİİ PIPëCḡPsP±PSPëPeP° C,P° P°PrCḡPμCfP° PjC-CfC†Cİİ PİCḡPsPIP°PrP¶PμPSPSCİİ PNëPsPiPs PrC-CİP»CHPSPsCfC,C-.

P’CfP»CHPIP°Cḡ PhP»PμPeCfP°PSPrCḡP° PњP°PePμPrPsPSCfCHPePsPiPs, 12, PŸPePsPİbḡ™C” , 1000, P PμCfPiCfP±P»C-PeP° PμC-PIPSC-C†PSP° PњP°PePμPrPsPSC-Cİİ.

Boulevard Aleksandar Makedonski 12, Skopje, 1000, Republic of North Macedonia.