Emtrivir
Emtricitabine/Tenofovir disoproxil fumarate
Tablets 200 mg/300 mg

1. Nama Produk Obat
Tablet salut selaput **Emtrivir**
Tenofovir Disoproxil Fumarate/Emtricitabine 300 mg/200 mg

2. Komposisi
Setiap tablet salut selaput mengandung:

Tenofovir Disoproxil Fumarate	300 mg
Emtricitabine	200 mg

3. Bentuk Sediaan
Bewarna biru, berbentuk seperti kapsul, biconvex, tablet salut selaput dengan cetakan "L 24" pada satu sisi dan polos pada sisi yang lain.
Tidak ada garis bagi. Tablet tidak boleh dibagi.

4.1. Mekanisme Kerja
Mekanisme Kerja
Emtricitabine: Emtricitabine, analog nukleosida sintetik cytidine, difosforilasi melalui enzim seluler untuk membantuk emtricitabine 5'triphosphate. Emtricitabine 5'triphosphate menghambat aktivitas reverse transcriptase (RT) HIV-1 dengan bersaing dengan deoxycytidine 5'triphosphate substrat alami dan dengan dimasukkan ke dalam DNA virus yang baru muncul sehingga mengakibatkan terputusnya rantai. Emtricitabine 5'triphosphate merupakan inhibitor lemah polimerase DNA mamalia α, β dan polimerase DNA mitokondria λ.
Aktivitas antivirus
Emtricitabine dan Tenofovir Disoproxil Fumarate: Dalam studi kombinasi yang mengevaluasi aktivitas antivirus biakan sel emtricitabine dan tenofovir bersama-sama, teramati adanya efek antivirus sinergis.
Emtricitabine: Aktivitas antivirus emtricitabine terhadap isolat HIV-1 laboratorium dan isolat HIV-1 klinis dinilai dalam garis sel limfoblastoid, garis sel MAGI-CCR5, dan sel mononuklear darah perifer. Nilai konsentrasi efektif 50% (EC50) untuk emtricitabine berada dalam rentang 0,0013 - 0,64 μM (0,0003-0,158 μg/ml). Dalam studi kombinasi obat emtricitabine dengan NRTI (abacavir, lamivudine, stavudine, zalcitabine, zidovudine), non-nucleoside reverse transcriptase inhibitor (delavirdine, efavirenz, nevirapine) dan protease inhibitor (amprenavir, nelfinavir, ritonavir, saquinavir), teramati adanya tambahan efek sinergis. Emtricitabine menunjukkan aktivitas antivirus dalam biakan sel terhadap nilai HIV-1 clades A, B, C, D, E, F, dan G (Ec50) berkisar antara 0,007 - 0,075 μM) dan menunjukkan aktivitas spesifik strain terhadap HIV-2 (nilai Ec50 berkisar dari 0,007-1,5 μM).
Tenofovir Disoproxil Fumarate: Aktivitas antivirus Tenofovir terhadap isolat HIV-1 laboratorium dan isolat HIV-1 klinis dievaluasi dalam garis sel limfoblastoid, sel monosit/makrofag primer dan limfosit darah perifer. Nilai Ec50 untuk tenofovir berada dalam rentang 0,04-8 μM. Dalam studi kombinasi obat tenofovir dengan nukleosida reverse transcriptase inhibitor (abacavir, didanosine, lamivudine, stavudine, zalcitabine, zidovudine), non nucleoside reverse transcriptase inhibitor (delavirdine, efavirenz, nevirapine) dan protease inhibitor (amprenavir, indinavir, nelfinavir, ritonavir, saquinavir), aditif dalam biakan sel terhadap HIV-1 clades A, B, C, D, E, F, G, dan 0 (nilai Ec50 berkisar antara 0,55-2,2 μM) dan menunjukkan aktivitas spesifik strain HIV-2 (nilai Ec50 berkisar antara 1,6 μM hingga 5,5 μM).
Resistensi
Emtricitabine dan Tenofovir Disoproxil Fumarate: Isolat HIV-1 dengan penurunan kerentanan terhadap kombinasi emtricitabine dan tenofovir dipilih dalam biakan sel. Analisis genotipik terhadap isolat ini mengidentifikasi substitusi asam amino M184V/1 dan/atau K65R dalam RT virus.
Dalam studi klinis terhadap pasien yang tidak menerima pengobatan (Studi 934, lihat studi klinis 14.1), analisis resistensi dilakukan pada isolat HIV-1 dari semua pasien kegagalan virologi dikonfirmasi dengan > 400 copy/ml HIV RNA HIV-1 pada minggu ke-144 atau penghentian dini. Perkembangan substitusi terkait resistensi efavirenz paling sering terjadi dan mirip antara kelompok pengobatan. Substitusi asam amino M184V, terkait dengan resistensi terhadap EMTRIVA dan lamivudine, teramati pada 2/19 isolat pasien yang dianalisis dalam kelompok zidovudine/lamivudine. Selama 144 minggu studi 934, tidak ada pasien yang mengembangkan substitusi K65R yang terdeteksi dalam HIV-1 mereka sebagaimana dianalisis melalui analisis genotip standar.
Emtricitabine: Isolat resisten Emtricitabine HIV-1 telah dipilih dalam biakan sel dan *in vivo*. Analisis genotipik terhadap isolat ini menunjukkan bahwa berkurangnya kerentanan terhadap emtricitabine dikaitkan dengan substitusi pada gen HIV-1 RT pada kodon 184 yang menghasilkan substitusi asam amino metionin melalui valin atau isoleusin (M184V/I).
Tenofovir Disoproxil Fumarate: HIV-1 isolat dengan penurunan kerentanan terhadap tenofovir telah dipilih dalam biakan sel. Virus-virus ini mengekspresikan substitusi K65R di kelompok TENOFOVIR DISOPROXIL FUMARATE hingga 144 minggu: 7 terjadi dalam 48 minggu pertama pengobatan dan 1 pada minggu ke-96. Pada pasien yang menerima pengobatan, 14/304 (5%) isolat dari pasien yang gagal TENOFOVIR DISOPROXIL FUMARATE sampai minggu ke 96 menunjukkan > 1,4 kali lipat (median 2,7) penurunan kerentanan terhadap tenofovir. Analisis genotipik terhadap isolat yang resisten menunjukkan substitusi pada gen HIV-1 RT dalam substitusi asam amino K65R.
Resistensi Silang
Emtricitabine dan Tenofovir Disoproxil Fumarate: Resistensi silang antara nucleoside reverse transcriptase inhibitor (NRTI) telah dikenali. Substitusi M184V/I dan/atau substitusi K65R dalam biakan sel dengan kombinasi emtricitabine dan tenofovir juga teramati pada beberapa isolat HIV-1 dari subjek yang gagal dengan pengobatan tenofovir yang dikombinasikan dengan lamivudine atau emtricitabine, dan abacavir atau didanosine. Oleh karena itu, resistensi silang di antara obat-obat ini dapat terjadi pada pasien yang virusnya memiliki salah satu atau kedua substitusi asam amino ini.
Emtricitabine: isolat (M184V/I) resisten-emtricitabine yang diisolasi memiliki resistensi silang terhadap lamivudine dan zalcitabine tetapi tetap memiliki kerentanan dalam biakan sel terhadap didanosin, stavudine, tenofovir, zidovudine dan NNRTI (delavirdine, efavirenz, dan nevirapine). HIV-1 terisolasi yang mengandung substitusi K65R, dipilih *in vivo* melalui abacavir, didanosine, tenofovir dan zalcitabine, menunjukkan penurunan kerentanan terhadap penghambatan oleh emtricitabine. Virus yang mengandung substitusi yang memiliki penurunan kerentanan terhadap stavudine dan zidovudine (M41L, D67N, K70R, L210W, T215Y/F, K219Q/E), atau didanosine (L74V) tampak tetap sensitif terhadap emtricitabine. HIV-1 yang mengandung substitusi K103N yang terkait dengan resistensi terhadap NNRTI tampak rentang terhadap emtricitabine.
Tenofovir Disoproxil Fumarate: HIV-1 yang diisolasi dari pasien yang HIV-1nya menunjukkan rata-rata 3 substitusi asam amino RT terkait zidovudine (M41L, D67N, K70R, L210W, T215Y/F atau K219Q/E/N) menunjukkan penurunan 3,1 kali lipat dalam hal kerentanannya terhadap tenofovir. HIV-1 resistan-multinucleoside dengan substitusi insersi ganda T69S di dalam RT menunjukkan penurunan kerentanan terhadap tenofovir.

5. Indikasi Terapeutik
Emtivir diindikasikan dalam kombinasi dengan agen antiretroviral lainnya (seperti non-nucleoside reverse transcriptase inhibitor atau penghambat protease) untuk pengobatan infeksi HIV-1 pada orang dewasa sebagai pengobatan lini kedua.
Hal-hal berikut harus dipertimbangkan ketika memulai terapi dengan Emtrivir untuk pengobatan infeksi HIV-1:
- Emtrivir tidak dianjurkan untuk digunakan sebagai komponen rejimen triple nukleosida.
- Emtrivir tidak boleh diberikan bersamaan dengan obat yang mengandung Tenofovir Disoproxil Fumarate atau Lamivudine (Lihat Peringatan dan Tindakan Pencegahan)
- Pada pasien yang mempunyai pengalaman dengan pemakaian antiretroviral, menerima pengobatan, penggunaan Emtrivir harus dipandu dengan pengujian laboratorium dan riwayat pengobatan

6. Dosis dan Pemberian
Dosis yang Direkomendasikan
Dosis Emtrivir adalah satu tablet (mengandung 300 mg Tenofovir Disoproxil Fumarate dan 200 mg Emtricitabine) sekali sehari yang dikonsumsi secara oral dengan atau tanpa makanan.
Penyesuaian Dosis untuk Gangguan Ginjal
Peningkatan paparan obat secara bermakna terjadi ketika emtricitabine atau tenofovir disoproxil fumarate diberikan pada pasien dengan gangguan ginjal sedang sampai berat. Oleh karena itu, interval pemberian dosis Emtrivir harus disesuaikan pada pasien dengan bersihan kreatinin 30-49 mL/menit sesuai anjuran pada tabel 1.
Anjuran interval pemberian dosis ini didasarkan pada pemodelan data farmakokinetik dosis tunggal pada pasien yang tidak terinfeksi HIV. Keamanan dan keefektifan dari rekomendasi penyesuaian interval pemberian dosis ini belum dievaluasi secara klinis pada pasien dengan gangguan ginjal sedang, oleh karena itu respons klinis terhadap pengobatan dan fungsi ginjal harus dipantau secara ketat pada pasien ini.
Tidak diperlukan penyesuaian dosis bagi pasien dengan gangguan ginjal ringan (bersihan kreatinin 50-80 mL/menit). Pemantauan rutin bersihan kreatinin yang dihitung dan fosfor serum harus dilakukan pada pasien dengan gangguan ginjal ringan.
Tabel 1. Penyesuaian Dosis bagi Pasien dengan Bersihan Kreatinin yang Berubah

	Bersihan Kreatinin (mL/min)*		
	≥ 50	30-49	< 30 (termasuk pasien yang membutuhkan hemodialisis)
Interval Pemberian Dosis yang Direkomendasikan	Setiap 24 jam	Setiap 48 jam	Tidak boleh diberikan

* Dihitung menggunakan berat badan ideal (ramping)

7. Kontraindikasi
Hipersensitif terhadap emtricitabine, tenofovir disoproxil fumarate, atau terhadap salah satu eksipien obat ini.

8. Peringatan Khusus dan Tindakan Pencegahan Penggunaan
8.1. Asidosis Laktat/Hepatomegali Berat dengan Stainosis
Asidosis laktat dan hepatomegali berat dengan stainosis, termasuk kasus fatal, telah dilaporkan dengan penggunaakn analog nukleosdia, termasuk Tenofovir Disoproxil Fumarate, komponen Emtrivir, dikombinasikan dengan ARV lain. Sebagian besar kasus-kasus ini terjadi pada wanita. Obesitas dan paparan nkleosida yang berkepanjangan dapat menjadi faktor risiko. Perhatian khusus harus diberikan ketika memberikan analog nukleosida pada pasien dengan faktor risiko penyakit hati yang diketahui; Namun, kasus ini juga telah dilaporkan pada pasien tanpa adanya faktor risiko yang diketahui. Pengobatan dengan Emtrivir harus dihentikan pada setiap pasien yang menunjukkan temuan klinis atau temuan laboratorium yang menunjukkan asidosis laktat atau hepatotoksisitas yang muncul (yang mungkin termasuk hepatomegali dan steatosis bahkan tanpa adanya tanda peningkatan transaminase).
8.2. Pasien koinfeksi HIV-1 dan HBV
Dianjurkan agar semua pasien dengan HIV-1 diuji untuk mengetahui keberadaan virus hepatitis B kronis (HBV) sebelum memulai terapi antiretroviral. Emtrivir tidak disetujui untuk pengobatan infeksi HBV kronis dan keamanan dan efikasi Emtrivir belum ditetapkan pada pasien dengan koinfeksi HBV dan HIV-1. Eksaserbasi Hepatitis B akut yang berat telah dilaporkan pada pasien dengan koinfeksi HBV dan HIV-1 dan pengobatan dengan Emtrivir dihentikan. Pada beberapa pasien yang terinfeksi HBV dan diobati dengan Emtricitabine (komponen Emtrivir), eksaserbasi Hepatitis B dikaitkan dengan dekompendasi hati dan gagal hati. Pasien dengan koinfeksi HIV-1 dan HBV harus dipantau secara ketat dengan tindak lanjut klinis dan laboratorium setidaknya selama beberapa bulan setelah menghentikan pengobatan dengan Emtrivir. Jika sesuai, pemberian terapi anti-hepatitis B mungkin dapat dibenarkan.
8.3. Onset Baru yang Memperburuk Kerusakan Ginjal
Emtricitabine dan tenofovir terutama dieliminasi oleh ginjal. Kerusakan ginjal, termasuk kasus gagal ginjal akut dan sindrom Fanconi (cedera tubulus ginjal dengan hipofosfatemia berat), telah dilaporkan dengan penggunaan Tenofovir Disoproxil Fumarate.
Dianjurkan agar bersihan kreatinin diperiksa pada semua pasien sebelum memulai terapi dan sebagai pengobatan klinis yang tepat selama terapi dengan Emtrivir.

Pemantauan rutin bersihan kreatinin yang dihitung dan fosfor serum harus dilakukan pada pasien yang berisiko mengalami gangguan ginjal. Penyesuaian interval pemberian dosis Emtrivir dan pemantauan ketat fungsi ginjal direkomendasikan pada semua pasien dengan klirens kreatinin 30-49 mL/menit. Belum tersedia data keamanan atau khasiat pada pasien dengan gangguan ginjal yang menerima Emtrivir sesuai panduan pemberian dosis, sehingga perlu diperhitungkan potensi manfaat terhadap potensi risiko toksisitas ginjal. Emtrivir tidak boleh diberikan pada pasien dengan bersihan kreatinin <30 mL/menit atau pasien yang membutuhkan hemodialisis. Hindari penggunaan Emtrivir bersama dengan obat nefrotoksik.

8.4. Pemberian Bersamaan dengan Produk Lain

Emtrivir adalah kombinasi pemberian dosis tetap Tenofovir Disoproxil Fumarate dan Emtricitabine. Emtrivir tidak boleh digunakan bersamaan dengan Tenofovir Disoproxil Fumarate. Karena kemiripan antara Emtricitabine dan Lamivudine, Emtrivir tidak boleh digunakan bersamaan dengan obat lain yang mengandung Lamivudine lainnya, seperti Kombinasi Lamivudine/Zidovudine, Lamivudine, Obat Kombinasi Abacavir Sulfate/Lamivudine, atau Obat kombinasi Abacavir Sulfate/Lamivudine/Zidovudine.

Emtrivir tidak boleh diberikan dengan Adefovir Dipifoxil.

8.5. Penurunan Kepadatan Mineral Tulang

Pemantauan Kepadatan Mineral Tulang atau *Bone Mineral Density (BMD)* harus dipertimbangkan untuk pasien terinfeksi HIV yang memiliki riwayat patah tulang patologis atau berisiko osteopenia. Meskipun efek suplementasi dengan kalsium dan vitamin D belum diteliti, suplementasi tersebut mungkin bermanfaat untuk semua pasien. Jika kelainan tulang dicurigai maka dapatkan konsultasi yang sesuai.

8.6. Redistribusi Lemak

Redistribusi/akumulasi lemak tubuh termasuk obesitas, pembesaran lemak dorsocervical (*buffalo hump*), pengecilan perifer, pengerutan wajah, pembesaran payudara, dan Kemunculan Sindrom Cushing telah diamati pada pasien yang menerima terapi antiretroviral. Mekanisme dan konsekuensi jangka panjang dari peristiwa tersebut saat ini tidak diketahui. Hubungan kausal belum ditetapkan.

8.7. Sindrom Rekonstitusi Kekebalan Tubuh

Sindrom pemulihan kekebalan tubuh telah dilaporkan pada pasien yang diobati dengan terapi kombinasi antiretroviral, termasuk Emtrivir. Selama fase awal kombinasi pengobatan antiretroviral, pasien yang memiliki respons sistem kekebalan tubuh dapat mengembangkan respons inflamasi terhadap infeksi oportunistik indolen atau residual (seperti infeksi *Mycobacterium avium,* cytomegalovirus, *Pneumocytis jirovecii pneumonia* (PCP), atau tuberculosis, yang mungkin memerlukan evaluasi dan pengobatan lebih lanjut.

9. Interaksi Obat

9.1. Didanosin

Pemberian bersamaan Emtrivir dan Didanosine harus dilakukan dengan hati-hati dan pasien yang menerima kombinasi ini harus dipantau secara ketat mengenai reaksi merugikan terkait dengan didanosine. Didanosine harus dihentikan pada pasien yang mengalami reaksi merugikan terkait didanosine.

Ketika Tenofovir Disoproxil Fumarate diberikan sebagai formulasi enterik meningkat secara signifikan. Mekanisme interaksi ini tidak diketahui. Konsentrasi didanosin yang lebih tinggi dapat mempotensiasi reaksi merugikan terkait dengan isanosin, termasuk pankreatitis, dan neuropati. Penekanan jumlah Cd4+ telah diamati pada pasien yang menerima Tenofovir DF dengan Didanosine 400 mg setiap hari.

Pada orang dewasa dengan berat >60 kg, dosis didanosine harus dikurangi menjadi 250 mg ketika digunakan bersamaan dengan Emtrivir. Data tidak tersedia untuk merekomendasikan penyesuaian dosis Didanosine untuk berat badan pasien <60 kg. Ketika digunakan bersamaan, Emtrivir dan Didanosine dapat diberikan dalam kondisi berpuasa atau dengan makanan ringan (<400 kkal, 20% lemak). Pemberian bersamaan didanosin dengan Emtrivir harus dalam kondisi berpuasa.

9.2. Atazanavir

Atazanavir telah terbukti meningkatkan konsentrasi tenofovir. Mekanisme interaksi ini tidak diketahui. Pasien yang menerima Atanazavir dan Emtrivir harus dihentikan pada pasien yang mengalami reaksi merugikan terkait Emtrivir.

Tenofovir Disoproxil Fumarate menurunkan AUC dan Cmax Atazanavir. Apabila digunakan bersamaan dengan Emtrivir, direkomendasikan agar Atazanavir diberikan dengan Ritonavir 100 mg. Atazanavir tanpa Ritonavir tidak boleh digunakan bersamaan dengan Emtrivir.

9.3. Lopinavir/Ritonavir

Lopinavir/Ritonavir telah terbukti meningkatkan konsentrasi Tenofovir. Mekanisme interaksi ini tidak diketahui. Pasien yang menerima Lopinavir/Ritonavir dan Emtrivir harus dipantau. Hentikan pengobatan dengan Emtrivir pada pasien yang mengalami reaksi merugikan.

9.4. Obat yang Mempengaruhi Fungsi Ginjal

Tenofovir dan Emtricitabine terutama diekskresikan melalui ginjal oleh kombinasi filtrasi glomerular dan sekresi tubular aktif. Tidak ada interaksi obat yang berkompetisi untuk diekskresikan melalui ginjal: namun demikian, penggunaan bersamaan Emtrivir dengan obat-obatan yang dieliminasi melalui sekresi tubular aktif dapat meningkatkan konsentrasi Emtricitabine, Tenofovir, dan/atau obat lain yang digunakan bersamaan. Seperti Acyclovir, Adefovir Dipifoxil, Cidofovir, Ganciclovir, Valacyclovir, dan Valganciclovir. Obat-obatan yang menurunkan fungsi ginjal dapat meningkatkan konsentrasi Emtricitabine dan/atau Tenofovir.

10. Penggunaan dalam Populasi Tertentu

10.1. Kehamilan

Tidak ada studi yang memadai terhadap wanita hamil, oleh karena itu, Emtrivir hanya digunakan selama kehamilan jika benar-benar diperlukan.

10.2. Ibu Menyusui

Ibu yang terinfeksi HIV-1 dianjurkan tidak menyusi bayi mereka untuk menghindari risiko penularan HIV setelah melahirkan. Tidak diketahui apakah Emtricitabine diekskresikan dalam ASI. Karena potensi penularan HIV-1 dan potensi reaksi reaksi merugikan pada bayi yang menyusu, ibu harus diinstruksikan untuk tidak boleh menyusui jika mereka menerima Emtrivir.

10.3. Penggunaan pada Anak

Emtrivir tidak direkomendasikan untuk pasien kurang dari 18 tahun karena keamanan dan efikasi-nya belum ditetapkan dalam kelompok usia ini.

10.4. Penggunaan pada Pasien Lanjut Usia

Secara umum, pemilihan dosis untuk pasien lanjut usia harus hati-hati, mengingat lebih tingginya frekuensi penurunan fungsi hati, ginjal, atau jantung, dan penyakit penyerta atau terapi obat lainnya.

10.5. Pasien dengan Gangguan Fungsi Ginjal

Dianjurkan modifikasi dosis Emtrivir pada pasien dengan bersihan kreatinin 30-49 mL/menit. Emtrivir tidak boleh digunakan pada pasien dengan klirens kreatinin <30 mL/menit dan pada pasien dengan penyakit ginjal stadium akhir yang memerlukan dialisis.

11. Efek pada Kemampuan Berkendara dan Menggunakan Mesin

Belum ada studi tentang efek pada kemampuan berkendara dan menggunakan mesin yang telah dilakukan. Namun, pasien harus diberitahu bahwa kejadian pusing telah dilaporkan selama pengobatan dengan Tenofovir Disoproxil Fumarate dan Emtricitabine.

12. Efek yang Tidak Diinginkan

Efek yang tidak diinginkan berikut dibahas di bagian lain dari pelabelan:

- Asidosis Laktat/Hepatomegali Berat dengan Stainosis
- Eksaserbasi Akut Parah Hepatitis B
- Onset Baru atau Kerusakan Ginjal yang Memburuk
- Penurunan kepadatan mineral tulang (lihat Peringatan dan Tindakan Pencegahan)
- Sindrom Rekonstitusi Kekebalan Tubuh (lihat Peringatan dan Tindakan Pencegahan)

13. Pengalaman Pasca Pemasaran

Reaksi merugikan berikut telah diidentifikasi selama penggunaan Tenofovir Disoproxil Fumarate pasca penggunaan. Tidak ada reaksi merugikan tambahan yang teridentifikasi selama penggunaan Emtricitabine pasca penggunaan. Karena reaksi pasca pemasaran dilaporkan secara sukarela dari populasi dengan ukuran yang tidak pasti, tidak selalu memungkinkan untuk memperkirakan dengan tepat frekuensi mereka dalam membentuk hubungan kausal untuk paparan obat.

- *Gangguan Sistem Kekebalan Tubuh*: Reaksi alergi
- *Gangguan Metabolisme dan Nutrisi*: Asidosis laktat, hipokalemia, hipofosfatemia
- *Gangguan Pernapasan, Toraks dan Mediastinum*: Dyspnoea
- *Gangguan Gastrointestinal*: Pankreatitis, peningkatan amilase, nyeri perut
- *Gangguan Hepatobiliari*: Hepatik steatosism hepatitis, peningkatan enzim hati (paling sering AST, ALT gamma GT)
- *Gangguan Kulit dan Jaringan Subkutan*: Rhabdomyolysis, osteomalacia (terbukti sebagai nyeri tulang dan yang dapat menyebabkan patah tulang), kelemahan otot, miopati
- *Gangguan Ginjal dan Urin*: Gagal ginjal akut, gagal ginjal, nekrosis tubular akut, sindrom Fanconi, tubulus ginjal proksimal, nefritis interstisial (termasuk kasus akut), diabetes insipidus nefrogenik, insufisiensi ginjal, peningkatan kreatinin, proteinuria, poliuria
- *Gangguan Umum dan Kondisi Tapak Pemberian*: Asthenia

Reaksi merugikan berikut dapat terjadi sebagai akibat dari tubulopati ginjal proksimal: rhabdomyolysis, osteomalacia, hipokalemia, kelemahan otot, miopati, hipofosfatemia.

14. Overdosis

Jika terjadi overdosis pasien harus dipantau untuk mengetahui toksisitas, dan pengobatan pendukung standar harus diterapkan sebagaimana diperlukan.

Emtricitabine: Tidak dilaporkan adanya reaksi merugikan yang parah dengan dosis tunggal emtricitabine 1200 mg.

Pengobatan hemodialisis menghilangkan sekitar 30% dari dosis emtricitabine selama periode dialisis 3 jam mulai dari 1,5 jam dosis emtricitabine (laju aliran darah 400 ml/menit dan tingkat aliran dialisat 600 ml/menit). Tidak diketahui apakah emtricitabine dapat dieliminasi dengan dialisis peritoneal.

Tenofovir Disoproxil Fumarate: Pengalaman Klinis Terbatas pada dosis yang lebih tinggi dari dosis terapi TENOFOVIR DISOPROXIL FUMARATE 300 mg tersedia. Tidak dilaporkan adanya reaksi merugikan yang parah dari tenofovir disoproxil fumarate 600 mg setelah pemberian kepada pasien secara oral selama 28 hari. Efek dari dosis yang lebih tinggi tidak diketahui.

Tenofovir secara efisien dieliminasi dengan hemodialisis dengan koefisien ekstraksi sekitar 54%. Setelah dosis tunggal 300 mg TENOFOVIR DISOPROXIL FUMARATE, sesi hemodialisis empat jam dihilangkan sekitar 10% dari Dosis tenofovir yang diberikan.

15. Daftar Eksipien

a. Inti tablet

Lactose monohydrate
Microcrystalline cellulose
Pre-gelatinized starch
Croscarmellose sodium
Colloidal silicon dioxide
Magnesium stearate

b. Salut film tablet:

Lactose monohydrate
Hypromellose
Titanium dioxide
Triacetin
FD&C Blue #2 / Indigo carmine alumunium lake

16. Inkompatibilitas: Tidak Ada

17. Penyimpanan: Simpan pada suhu di bawah 30°C. Lindungi dari cahaya. Gunakan dalam 30 hari setelah kemasan dibuka

18. Shelf-life: 24 bulan

19. Jenis dan Ukuran Wadah

Jenis Wadah: Dus, botol HDPE
Ukuran wadah : Botol @30 Tablet Salut Selaput

20. Pemegang Izin Edar

Diproduksi oleh: **Macleods Pharmaceuticals Limited**, Daman-India
Diimpor oleh: **PT. Sampharindo Retroviral Indonesia**, Semarang-Indonesia

21. Klasifikasi Obat: Obat Keras

22. Peringatan Khusus

HARUS DENGAN RESEP DOKTER

23. No. Reg:

Any other use is not authorized
The products are not authorized for supply to the Private Market

PATIENT INFORMATION LEAFLET

Information for the patient

Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets *
emtricitabine and tenofovir disoproxil fumarate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have questions about the medicine, ask your health care provider.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness seem to be the same as yours.
- If you get any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets is and what it is used for

Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets is a treatment for Human Immunodeficiency Virus (HIV) infection in adults and adolescents over 10 years of age weighing more than 30 kg.

To prevent the virus from becoming resistant Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets should always be given in combination with at least one other antiretroviral medicine.
Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets is used to reduce the risk of getting HIV-1 infection in adults and adolescents who are not HIV infected (i.e. HIV-negative) and are at high risk of getting infected with HIV. This is called oral pre-exposure prophylaxis (PrEP).

It should be used in combination with safer sex practices (see section 2).
Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets contains the active substances *emtricitabine* and *tenofovir disoproxil fumarate*. Both of these are *antiretroviral* medicines for the treatment of HIV infection. Emtricitabine is a *nucleoside reverse transcriptase inhibitor*. Tenofovir is a *nucleotide reverse transcriptase inhibitor.* Both active substances work by interfering with the normal working of an enzyme (reverse transcriptase) that is essential for the virus to reproduce itself.

* Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

2. What you need to know before you take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets

Do not take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets:

If you are allergic (hypersensitive) to emtricitabine, tenofovir, tenofovir disoproxil fumarate or any of the other ingredients of Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets listed at the end of this leaflet.

If this applies to you, tell your health care provider immediately and don't take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets.

Before taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets to reduce the risk of getting HIV:

Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets can only help reduce your risk of getting HIV **before** you are infected.

- **You must be HIV negative before you start to take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets to reduce the risk of getting HIV**. You must get tested to make sure that you do not already have HIV infection. Do not take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets to reduce your risk unless you are confirmed to be HIV negative. People who do have HIV must take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets in combination with other drugs.
- **Many HIV tests can miss a recent infection.** If you get a flu-like illness, it could mean you have recently been infected with HIV. These may be signs of HIV infection:
  - tiredness
  - fever
  - joint or muscle aches
  - headache
  - vomiting or diarrhoea
  - rash
  - night sweats
  - enlarged lymph nodes in the neck or groin

➢ **Tell your health care provider about any flu-like illness** – either in the month before starting Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets, or at any time while taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets.

Warnings and precautions

Talk to your health care provider before taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets.

While taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets to reduce the risk of getting HIV:

- Do not miss any doses of Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets, or stop taking it. Missing doses may increase your risk of getting HIV infection.
- Get tested for HIV regularly.
- If you think you were infected with HIV, tell your health care provider straight away. More tests may be necessary to make sure you are still HIV negative.

Just taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets may not stop you getting HIV.

- Always practice safer sex. Use condoms to reduce contact with semen, vaginal fluids, or blood.
- Do not share personal items that can have blood or body fluids on them, such as toothbrushes and razor blades.
- Do not share or re-use needles or other injection or drug equipment.
- Get tested for other sexually transmitted infections such as syphilis and gonorrhoea. These infections make it easier for HIV to infect you.

Ask your health care provider if you have any more questions about how to prevent getting HIV or spreading HIV to other people.

While taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets to treat HIV or to reduce the risk of getting HIV:

- **Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets may affect your kidneys**. Before and during treatment, your health care provider may order blood tests to measure kidney function. Tell your health care provider if you have had kidney disease, or if tests have shown kidney problems. If you have kidney problems, your health care provider may advise you to stop taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets or, if you already have HIV, to take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets less frequently. Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets is not recommended if you have severe kidney disease or are on dialysis.

  Bone problems (sometimes resulting in fractures) may also occur due to damage to kidney tubule cells (see section 4, Possible side effects).

- **Talk to your health care provider if you have a history of liver disease, including hepatitis.** Patients infected with HIV who also have liver disease (including chronic hepatitis B or C), who are treated with antiretrovirals, have a higher risk of severe and potentially fatal liver complications. If you have hepatitis B or C, your health care provider will carefully consider the best treatment regimen for you.
  - **Know your hepatitis B virus (HBV) infection status** before starting Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets. If you have HBV, there is a serious risk of liver problems when you stop taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets, whether or not you also have HIV. It is important not to stop taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets without talking to your health care provider: see section 3, If you stop taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets.
- **Talk to your health care provider if you are over 65.** Emtricitabine/tenofovir disoproxil fumarate has not been studied in patients over 65 years of age.
- **This medicine is not a cure for HIV infection.** While taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets you may still develop infections or other illnesses associated with HIV infection. You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your health care provider the precautions needed to avoid infecting other people.

Children

Other medicines and Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets
Tell your health care provider if you are taking any other medicines or have recently taken other medicines. Make sure you mention herbal medicines you might have been taking.

Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets is not for use in children under 10 years of age.

Other medicines and Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets

Do not take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets if you are already taking other medicines that contain the components of Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets (emtricitabine and tenofovir disoproxil fumarate) or any other antiviral medicines that contain tenofovir, tenofovir alafenamide, lamivudine or adefovir dipivoxil.

Taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets with other medicines that can damage your kidneys: it is especially important to tell your health care provider if you are taking any of these medicines, including

- aminoglycosides (for bacterial infection)
- amphotericin B (for fungal infection)
- foscarnet (for viral infection)
- ganciclovir (for viral infection)
- pentamidine (for infections)
- vancomycin (for bacterial infection)
- interleukin-2 (to treat cancer)
- cidofovir (for viral infection)
- non-steroidal anti-inflammatory drugs (NSAIDs, to relieve pain)

If you are taking another antiviral medicine called a protease inhibitor to treat HIV, your health care provider may order blood tests to closely monitor your kidney function.

It is also important to tell your health care provider if you are taking ledipasvir/sofosbuvir to treat hepatitis C infection.

Taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets with other medicines containing didanosine (for treatment of HIV infection): Taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets with other antiviral medicines that contain didanosine can raise the levels of didanosine in your blood and may reduce CD4 cell counts. Rarely, inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), which sometimes causes death, have been reported when medicines containing tenofovir disoproxil fumarate and didanosine were taken together. Your health care provider will carefully consider whether to treat you with combinations of tenofovir and didanosine.

- **Tell your health care provider** if you are taking any of these medicines. Tell your health care provider if you are taking, have recently taken or might take any other medicines.

Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets with food and drink and alcohol
You can take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets with food or between meals.

Pregnancy and breast-feeding
If you become pregnant or are planning to become pregnant, you must contact your health care provider to discuss the potential benefits and risks of taking this medicine to you and your child. Be sure to tell your health care provider immediately if you are or may be pregnant.

If you are interested in breastfeeding your baby, you should discuss the risks and benefits with your health care provider.

Driving and using machines
Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets can cause dizziness. If you feel dizzy while taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets, **do not drive** and do not use any hazardous tools or machines.

Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor or health care provider before taking this medicinal product.

3. How to take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets

Always take this medicine exactly as described in this leaflet or as your health care provider has told you. Check with your health care provider if you are not sure.

Always take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets and the doses exactly as your health care provider has told you. This is to make sure that your medicine is and remains fully effective. You should check with your health care provider if you are not sure. Do not change the dose unless your health care provider tells you to.

The dose for adolescents and adults is **one tablet each day**.

You can take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets with food or between meals.

Swallow Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets whole with water or another liquid.

If you cannot swallow the tablet, break or crush the tablet and add it to a small amount of liquid or semi-solid food. Swallow all the mixture immediately.

When used for HIV-treatment:
This product is not for use by children under 10 years of age or adolescents weighing less than 30 kg,
When used for reducing the risk of getting HIV-1 infection:
This product is not for use by children under 10 years of age or adolescents weighing less than 35 kg.

For treatment of established HIV-infection:
Your health care provider will prescribe Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets with at least one other antiretroviral medicine. Please refer to the patient information leaflets of the other antiretrovirals for guidance on how to take those medicines.

If your health care provider decides to stop one of the components of Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets or change the dose of this medicine, you may be given emtricitabine and/or tenofovir separately instead of the combined medicine or other medicines for the treatment of HIV infection.

If you have problems with your kidneys, your health care provider may advise you to take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets less frequently.

If you take more Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets than you should:
If you accidentally take too many Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets, contact your health care provider or nearest emergency department for advice. Take the tablet container with you so that you can easily describe what you have taken.

If you forget to take Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets:
It is important not to miss a dose of Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets. If you miss a dose of this medicine, take it as soon as you can, and then take your next dose at its regular time. However, if your next dose is due within 6 hours, do not take the missed dose. Wait and take the next dose at the usual time. Do not take a double dose to make up for a forgotten tablet.

If you vomit less than 1 hour after taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets, take another tablet. You do not need to take another tablet if you were sick more than 1 hour after taking this medicine.

If you stop taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets:

Don't stop taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets without your health care provider's advice. Stopping Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets may reduce the effectiveness of the treatment. Talk to your health care provider before you stop taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets for any reason, particularly if you are experiencing any side effects, have another illness, or if you think you are no longer at risk of getting infected with HIV.
Contact your health care provider before you restart taking Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets.

If you have hepatitis B or HIV and hepatitis B together (co-infection), it is very important not to stop your Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets treatment without talking to your health care provider first. Some patients have had blood tests or symptoms indicating that their hepatitis has got worse after stopping this medicine. You may require blood tests for several months after stopping treatment. Tell your health care provider immediately about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

If you have any further questions on the use of this product, ask your health care provider.

4. Possible side effects

Like all medicines, this medicine can cause side effects. Possible side effects of this medicine are listed below but they affect people differently and not everybody gets them.

The following side effects have been observed in patients who were treated for HIV-1 infection.

Possible serious side effects:

- **Lactic acidosis** (excess lactic acid in the blood) is a rare but potentially life-threatening side effect. Lactic acidosis occurs more often in women, particularly if they are overweight, and in people with liver disease. The following may be signs of lactic acidosis:
  - deep rapid breathing
  - drowsiness
  - feeling sick (nausea), being sick (vomiting)
  - stomach pain

➢ **If you think you may have lactic acidosis, get medical help immediately.**

- **Any signs of inflammation or infection**. In some patients with advanced HIV infection (AIDS) and a history of opportunistic infections (infections that occur in people with a weak immune system), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is thought that these symptoms are due to an improvement in the body's immune response, enabling the body to fight infections that may have been present with no obvious symptoms.
- **Autoimmune disorders**, when the immune system attacks healthy body tissue, may also occur after you start taking medicines to treat HIV infection. Autoimmune disorders may occur many months after the start of treatment. Look out for any symptoms of infection or other symptoms such as:
  - muscle weakness
  - weakness beginning in the hands and feet and moving up towards the trunk of the body
  - palpitations, tremor or hyperactivity

➢ **If you notice these or any symptoms of inflammation or infection, get medical help immediately.**

Possible side effects:

Very common side effects
(may affect more than 1 in 10 people)

- diarrhoea, being sick (vomiting), feeling sick (nausea)
- dizziness, headache
- rash
- feeling weak

Tests may also show:

- decreases in phosphate in the blood
- increased creatine kinase

Common side effects
(may affect up to 1 in 10 people)

- pain, stomach pain
- difficulty sleeping, abnormal dreams
- problems with digestion resulting in discomfort after meals, feeling bloated, flatulence
- rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions, itching, changes in skin colour including darkening of the skin in patches
- other allergic reactions, such as wheezing, swelling or feeling light-headed
  Tests may also show:
- low white blood cell count (a reduced white blood cell count can make you more prone to infection)
- increased triglycerides (fatty acids), bile or sugar in the blood
- liver and pancreas problems

Uncommon side effects
(may affect up to 1 in 100 people)

- pain in the abdomen (tummy) caused by inflammation of the pancreas
- swelling of the face, lips, tongue or throat
- anaemia (low red blood cell count)
- breakdown of muscle, muscle pain or weakness which may occur due to damage to the kidney tubule cells

Tests may also show:

- decreases in potassium in the blood
- increased creatinine in your blood
- changes to your urine

Rare side effects
(may affect up to 1 in 1,000 people)

- Lactic acidosis (see *Possible serious side effects*)
- fatty liver
- yellow skin or eyes, itching, or pain in the abdomen (tummy) caused by inflammation of the liver
- inflammation of the kidney, passing a lot of urine and feeling thirsty, kidney failure, damage to kidney tubule cells
- softening of the bones (with bone pain and sometimes resulting in fractures)
- back pain caused by kidney problems

Damage to kidney tubule cells may be associated with breakdown of muscle, softening of the bones (with bone pain and sometimes resulting in fractures), muscle pain, muscle weakness and decreases in potassium or phosphate in the blood.

- **If you notice any of the side effects listed above or if any of the side effects get serious**, talk to your health care provider.

The frequency of the following side effects is not known.

- **Bone problems**. Some patients taking combination antiretroviral medicines such as Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). Taking this type of medicine for a long time, taking corticosteroids, drinking alcohol, having a very weak immune system, and being overweight, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are:
- joint stiffness
- joint aches and pains (especially of the hip, knee and shoulder)
- difficulty with movement

➢ **If you notice any of these symptoms tell your health care provider.**

During treatment for HIV there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your health care provider will test for these changes.

Adults not infected with HIV and using tenofovir disoproxil fumarate/emtricitabine to reduce the risk of getting HIV-1 infection experienced in clinical trials no side effects other than those described above. The following side effects were reported in at least 2% of the participants and occurred slightly more frequently in the treatment group (as compared to placebo):
Headache, abdominal pain, weight decrease and syphilis (a sexually transmitted infection).

Reporting of side effects
If you get any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. If available, you can also report side effects directly through the national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets

Keep this medicine out of the sight and reach of children.

HDPE bottles: Store below 30°C, in dry place protected from light.
Alu-Alu blisters: Store below 25°C, in dry place protected from light.

Do not use this medicine after the expiry date stated on the pack after {EXP}. The expiry date refers to the last day of that month.

Do not use this medicine if you notice the medicine has changed color.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets contains
The active substance(s) are 200 mg emtricitabine and 300 mg tenofovir disoproxil fumarate (equivalent to 245 mg of tenofovir disoproxil or 136 mg of tenofovir).

The other ingredient(s) are:
Core tablet: Colloidal silicon dioxide, Croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose and pre-gelatinized starch

Film coat: FD&C Blue #2 / Indigo carmine aluminium lake, hypromellose, lactose monohydrate, titanium dioxide and triacetin

What Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets looks like and contents of the pack
Emtricitabine/Tenofovir Disoproxil Fumarate 200 mg/300 mg Tablets are blue coloured, capsule shaped, biconvex, film-coated tablets debossed "L 24" on one side of the tablet and plain on other surface.

The primary packs are:
White, round HDPE bottle, with 3 g silica gel sachet and pack insert, induction sealed with PP closure. Pack size: 30 tablets.

Alu-Alu blisters containing 10 tablets. 10 Blisters per carton.

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For any information about this medicine, contact the supplier.

This leaflet was first revised in February 2017.
Section 6 updated in June 2019

Detailed information on this medicine is available on the World Health Organization (WHO) web site:
https://extranet.who.int/prequal