GILEAD | Medical Information

Descovy for PrEP® (FTC/TAF) Switching from FTC/TDF for PrEP

This document is in response to your request for information regarding switching to Descovy for PrEP® (emtricitabine/tenofovir alafenamide [FTC/TAF] for HIV-1 pre-exposure prophylaxis) from Truvada for PrEP® (emtricitabine/tenofovir disoproxil fumarate [FTC/TDF] for HIV-1 pre-exposure prophylaxis).

Some data may be outside of the US FDA-approved Prescribing Information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

Summary

Clinical Data

Daily FTC/TAF demonstrated non-inferior efficacy to FTC/TDF for HIV-1 PrEP among adult MSM and TGW in the phase 3 DISCOVER trial at both the primary and Week 96 analyses.[1-4]

- HIV incidence rates were low through Week 48 of the open label phase (FTC/TAF: 0.09 per 100 PY; FTC/TDF → FTC/TAF: 0.05 per 100 PY).[4]
- Improvements in bone and renal biomarkers were also observed in those who switched from FTC/TDF → FTC/TAF in the open label extension.[3,4]

Product Labeling

FTC/TAF for HIV-1 PrEP[5]

FTC/TAF is indicated in at-risk adults and adolescents weighing ≥35 kg for PrEP to reduce the risk of HIV-1 infection from sexual acquisition, excluding individuals at risk from receptive vaginal sex. Individuals must have a negative HIV-1 test immediately prior to initiating FTC/TAF for HIV-1 PrEP.

Limitations of Use: The indication does not include use of FTC/TAF in individuals at risk of HIV-1 from receptive vaginal sex because effectiveness in this population has not been evaluated.

FTC/TDF for HIV-1 PrEP[6]

FTC/TDF is indicated in at-risk adults and adolescents weighing ≥35 kg for PrEP to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test immediately prior to initiating FTC/TDF for HIV-1 PrEP.

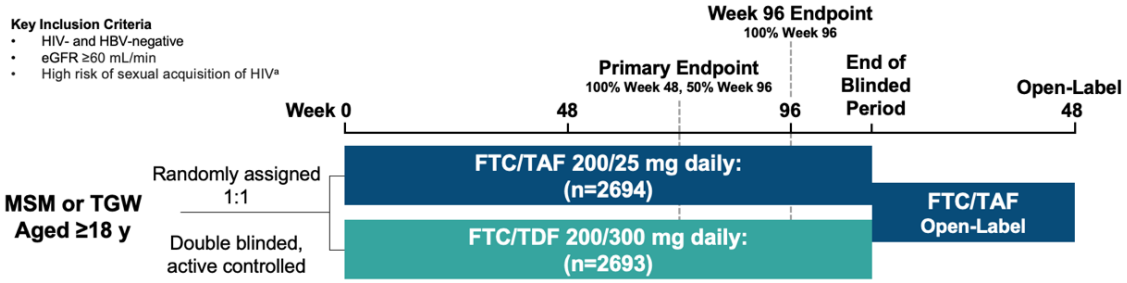
Clinical Data

DISCOVER: Once Daily FTC/TAF vs FTC/TDF for HIV-1 PrEP in MSM and TGW

Study Design and Demographics

DISCOVER is a phase 3, multinational study in 5387 HIV-negative adult MSM and TGW evaluating the safety and efficacy of FTC/TAF vs FTC/TDF for HIV-1 PrEP. Figure 1 below includes the study design and key inclusion criteria. Prior use of FTC/TDF for HIV-1 PrEP was allowed.[1,3,7]

Figure 1. DISCOVER Study Design[1,3,7]



[a]High risk defined as ≥2 episodes of condomless anal intercourse with ≥2 unique male partners of HIV-positive or unknown HIV status within the previous 12 weeks, or a documented history of syphilis, rectal gonorrhea, or rectal chlamydia in the previous 24 weeks.

The primary measured outcome was the incidence of HIV-1 per 100 PY after all participants had ≥48 weeks of follow-up and ≥50% of participants had 96 weeks of follow-up.[1] All participants were unblinded after 96 weeks, and participants in both arms were offered the opportunity to continue on or switch to once-daily FTC/TAF for an additional 48 weeks.[1,7]

Participant baseline characteristics were similar between the FTC/TAF and FTC/TDF arms, including risk factors for HIV acquisition (Table 1).[1]

Table 1. Baseline Demographics and HIV Risk Factors[1,2]

	FTC/TAF (n=2694)	FTC/TDF (n=2693)
Baseline Demographics		

	FTC/TAF (n=2694)	FTC/TDF (n=2693)
Median age, years (range)	34 (18–76)	34 (18–72)
Race, n (%)		
White	2264 (84)	2247 (84)
Black[a]	240 (9)	234 (9)
Asian	113 (4)	120 (4)
Hispanic or Latinx ethnicity, n (%)	635 (24)	683 (25)
Proportion TGW, n (%)	45 (2)	29 (1)
Sexual orientation, %		
Gay	92	91
Straight	1	1
Bisexual	6	8
Other	1	<1
Region, %		
USA	59	60
EU	34	33
Canada	7	6
HIV Risk Factors, %		
>2 receptive condomless anal sex, past 12 weeks	62	60
Rectal gonorrhea, past 24 weeks	10	10
Rectal chlamydia, past 24 weeks	13	12
Syphilis, past 24 weeks	9	10
Recreational drug use, past 12 weeks	67	67
Binge drinking[b]	23	22
Taking FTC/TDF for HIV-1 PrEP at baseline	17	16

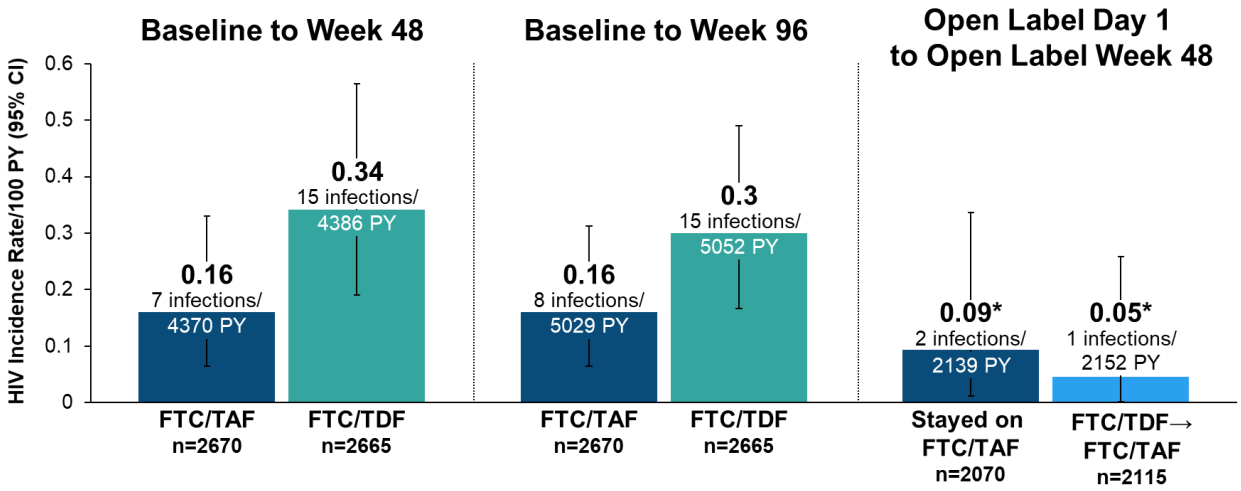
[a] Includes mixed Black race.
[b] ≥6 drinks on ≥1 occasion, at least monthly.

Efficacy Results

The primary endpoint analysis had a total follow-up of 8756 PY (4370 PY of FTC/TAF and 4386 PY of FTC/TDF) and included data from all participants with ≥48 weeks of follow-up and ≥50% of participants with 96 weeks of follow-up. Across FTC/TAF and FTC/TDF arms, there were a total of 22 HIV infections (7 vs 15, respectively) for an HIV incidence rate of 0.16/100 PY vs 0.34/100 PY, respectively. The incidence rate ratio between the FTC/TAF and FTC/TDF arms was 0.47 (95% CI: 0.19–1.15), and the upper bound of the 95% CI was less than the non-inferiority margin of 1.62, thus meeting the non-inferiority criteria.[1]

From Day 1 of the open label phase to Week 48 of the open label phase, there were a total of 3 HIV infections (FTC/TAF, n=2; FTC/TDF→FTC/TAF, n=1), for an HIV incidence rate of 0.09 per 100 PY in the FTC/TAF group and 0.05 per 100 PY in the FTC/TDF→FTC/TAF group (Figure 2). The HIV incidence rates were similar between the two study arms.[4] Of all HIV infections from baseline to Week 144, five participants had suspected baseline infections, and low levels of TFV-DP were found in 19 participants on DBS analysis.[8,9]

Figure 2. Incidence Rates of HIV Infection from Baseline to Week 144[4]



*During the open label phase, 1 additional participant in each group had a positive quantitative HIV nucleic acid amplification test that was later confirmed to be a false positive.

Safety Results

Bone Safety

In the small group of participants (n=20) with baseline FTC/TDF use, no statistically significant changes were seen when comparing hip and spine BMD in participants on FTC/TAF compared to FTC/TDF. Mean percent BMD change in the hip and spine were significantly different between the 2 arms, favoring FTC /TAF among participants without baseline FTC/TDF use. (Table 2).[10]

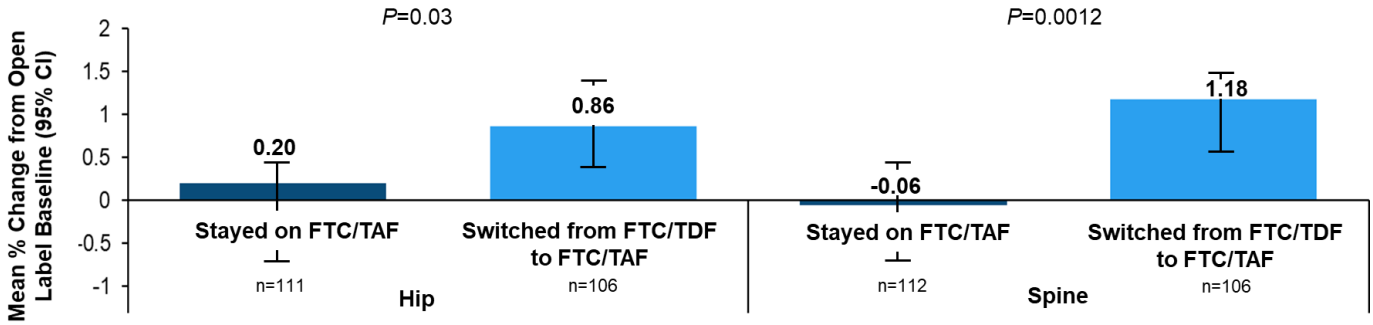
Table 2. Subanalyses of BMD (Mean % Change from Baseline) Substudy at Week 96[10]

BMD Cohort	Location	n	FTC/TAF	FTC/TDF	*P*-Value
Campbell Subanalysis[10]					
Baseline FTC/TDF	Hip	20[a]	+1.8	+1.4	0.75
	Spine	20[b]	+0.9	-1.2	0.13
No Baseline FTC/TDF	Hip	124[c]	+0.4	-1.4	<0.001
	Spine	125	+0.8	-1.5	<0.001

[a]n=20 in baseline FTC/TDF→FTC/TAF group, n=16 in baseline FTC/TDF→FTC/TDF group. [b]n=20 in baseline FTC/TDF→FTC/TAF group, n=17 in baseline FTC/TDF→FTC/TDF group. [c]n=124 in no baseline FTC/TDF→FTC/TAF group, n=122 in no baseline FTC/TDF→FTC/TDF group.

On Day 1 of the open label phase, which began 96 weeks after the blinded phase, hip and spine BMDs were not significantly different between study arms. At Week 48 of the open label phase, participants who switched from FTC/TDF to FTC/TAF had statistically significant increases in hip and spine BMD compared to those who remained on FTC/TAF (Figure 3).[4]

Figure 3. Changes in BMD at Week 48 Open Label Phase[4]



Please note, the long-term clinical significance of the BMD changes is not known.[5]

Renal Safety

On Day 1 of the open label phase, there were significant differences in renal biomarkers between participants who received FTC/TAF and those who received FTC/TDF during the blinded phase of the study (Table 3).[4]

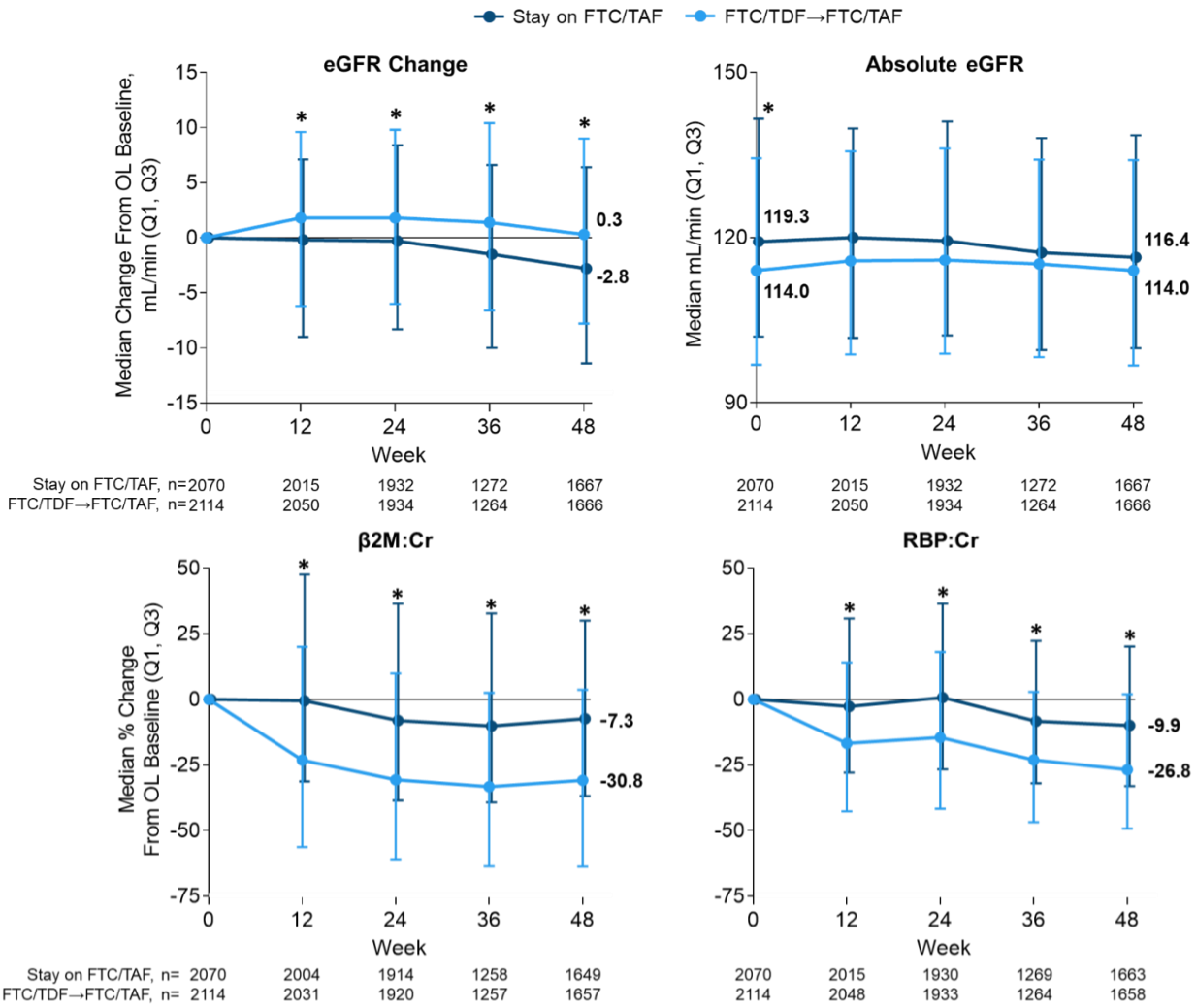
Table 3. Renal Biomarkers on Day 1 of the Open Label Phase[4]

Renal Biomarkers	Stayed on FTC/TAF	FTC/TDF→FTC/TAF	*P*-Value*
$eGFR_{CG}$, median (Q1, Q3), mL/min	119.3 (102, 141.6)	114 (96.9, 134.4)	<0.0001
β2M:Cr, median (Q1, Q3), µg/g	72.2 (51.1, 106.6)	99.3 (63.8, 202.9)	<0.0001
RBP:Cr, median (Q1, Q3), µg/g	102 (74.9, 146.8)	124.8 (88.6, 192.8)	<0.0001

*Calculated using the Cochran–Mantel–Haenszel test. Abbreviations: β2M=beta-2-microglobulin; $eGFR_{CG}$=estimated glomerular filtration rate by Cockcroft-Gault; RBP=retinol-binding protein

At Week 48 of the open label phase, participants who switched from FTC/TDF to FTC/TAF had significantly greater improvements in renal biomarkers compared to participants who stayed on FTC/TAF (Figure 4).[4]

Figure 4. Renal Outcomes at Week 48 of Open Label Phase[4]



*Calculated using the Cochran–Mantel–Haenszel test with mean scores to compare the 2 study arms.

Please note, the long-term clinical significance of these renal laboratory changes on adverse reaction frequencies between FTC/TAF and FTC/TDF is not known.[5]

Hepatic Safety Results

On Day 1 of the open label phase, HDL and LDL levels were significantly higher in participants who received FTC/TAF compared to those who received FTC/TDF during the blinded phase of the study (Table 4).[4]

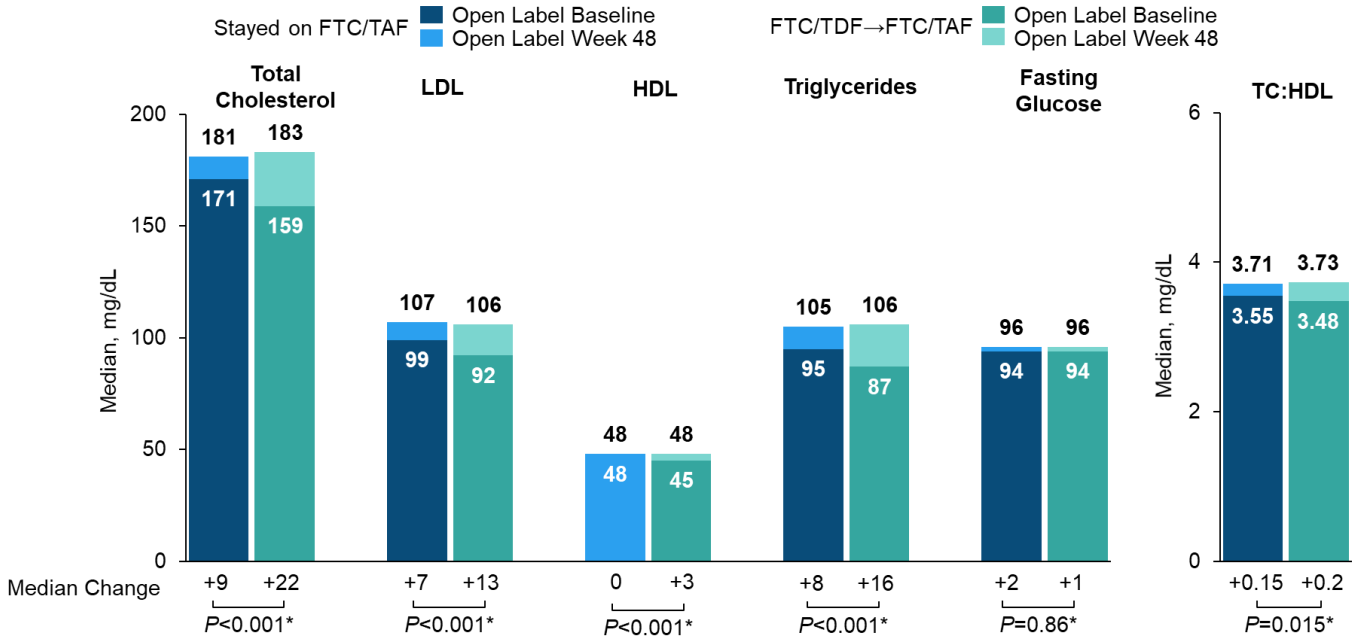
Table 4. Metabolic Indicators on Day 1 of the Open Label Phase[4]

Metabolic Indicators	Stayed on FTC/TAF	FTC/TDF→FTC/TAF	*P*-Value*
LDL, median (Q1, Q3), mg/dL	99 (80, 120)	92 (75, 113)	<0.0001
HDL, median (Q1, Q3), mg/dL	48 (40, 57)	45 (38, 54)	<0.0001

*Calculated with a 2-sided Wilcoxon rank sum test.

At Week 48 of the open label phase, median changes from baseline in TC, LDL, HDL, triglycerides, and TC:HDL ratio were significantly greater in participants switching from FTC/TDF to FTC/TAF compared to those remaining on FTC/TAF (Figure 5).[4]

Figure 5. Median Absolute Values and Changes in Fasting Lipid Levels at Week 48 of Open Label Phase[4]



*P-values were calculated with a 2-sided Wilcoxon rank sum test.

Weight Change

In both arms, approximately 50% of participants had a BMI in the overweight category at baseline. Median weight changes for participants in the FTC/TAF vs FTC/TDF arm, respectively, were +1 kg vs 0 kg (P<0.001) at Week 48, and +1.7 kg vs +0.5 kg (P<0.0001) at Week 96.[3,11] Median weight increase was observed across all study arms regardless of baseline PrEP use.[3] From Day 0 of the open label phase through Week 48, participants who stayed on FTC/TAF had a median weight change of +1.2 kg, and participants who switched from FTC/TDF to FTC/TAF had a median weight change of +2 kg (P<0.001).[4]

References

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2. Ruane P, Clarke A, Post FA, et al. Phase 3 Randomized, Controlled DISCOVER Study of Daily F/TAF or F/TDF for HIV Pre-exposure Prophylaxis: Week 96 Results [Poster PE3/16]. Paper presented at: 17th European AIDS Conference; 06-09 November, 2019; Basel, Switzerland.
3. Ogbuagu O, Ruane PJ, Podzamczer D, et al. Long-term safety and efficacy of emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet HIV.* 2021;8:e397-e407.

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Abbreviations

β2M=β2-microglobulin
CG=Cockcroft-Gault
Cr=creatinine
eGFR=estimated glomerular filtration rate
FTC=emtricitabine
MSM=men who have sex with men
OL=open-label
OLE=open-label extension
PrEP=pre-exposure prophylaxis
RBP=retinol-binding protein
TAF=tenofovir alafenamide
TDF=renofovir disoproxil fumarate
TGW=transgender women

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Descovy US Prescribing Information available at:
www.gilead.com/-/media/files/pdfs/medicines/hiv/descovy/descovy_pi

Follow Up

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☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

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🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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