

FOR ADULTS WITH ADVANCED PARKINSON'S DISEASE¹

MORE ONAPGO™ TIME



Explore a different route
for more GOOD ON time¹



INDICATION

ONAPGO is indicated for the treatment of motor fluctuations in adults with advanced Parkinson's Disease (PD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Concomitant use of ONAPGO with 5HT₃ antagonists is contraindicated based on reports of profound hypotension and loss of consciousness when ONAPGO was administered with ondansetron.

ONAPGO is contraindicated in patients who have demonstrated hypersensitivity/allergic/anaphylactic reaction to it or any of its excipients, including sulfite (i.e., sodium metabisulfite).

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



All photos within this piece are actor portrayals unless otherwise noted.

INCONSISTENT MOTOR CONTROL

remains a challenge in Parkinson's disease^{2,3}

Motor fluctuations continue to disrupt daily life despite:

- Higher doses of levodopa (LD)^{2,3}
- More frequent doses of LD closer together^{2,3}
- Adjunctive therapies^{2,3}



“ My days feel unpredictable with the ups and downs.
I want to feel more in control of my day. ”

—SCOTT, 59, small business owner

~50%

of patients in an MJFF survey* reported that OFF time causes them to avoid or stop activities they can perform while ON⁴

*Michael J. Fox Foundation; N>3000.

CHALLENGES ALONG THE ROUTE

to more continuous control of motor fluctuations⁵⁻⁸

PD progression and pulsatile delivery of treatments contribute to daily variability, making management a challenge.⁵



GI DYSFUNCTION

GI dysmotility, variable absorption, and competitive protein transport across the intestinal wall lead to lower plasma concentrations of LD⁶⁻⁸



BLOOD-BRAIN BARRIER (BBB)

Protein competition at the BBB and short half-life of levodopa (~90 minutes) limit the amount entering the brain^{5,7,8}



PULSATILE STIMULATION

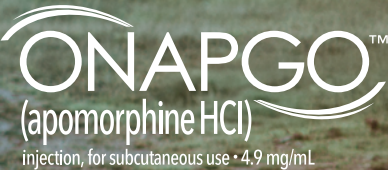
Degeneration of presynaptic dopaminergic neurons impairs the brain's ability to buffer fluctuations in dopamine. Normally, these neurons convert LD to dopamine, then store and release it in a controlled manner to maintain stable levels⁵

Do your advanced
PD patients **experience**
daily OFF time disruptions
despite adjustments to
oral therapies?



**IT'S TIME
TO EXPLORE A
DIFFERENT ROUTE^{1,3}**

EXPLORE A DIFFERENT ROUTE TO MORE GOOD ON TIME¹



CONSISTENT CONTROL

Significant **reduction in daily OFF time** accompanied by a significant **increase in GOOD ON time**^{*1}

^{*}GOOD ON time=ON time without troublesome dyskinesia.

CONTINUOUS TREATMENT

Flexible, all-day[†] infusion with **individualized dosing**¹

[†]Waking day (e.g., 16 h)



ONAPGO is a nonsurgical subcutaneous treatment option that is generally worn during the waking day.^{1,9}

OVER 30 YEARS OF CLINICAL EXPERIENCE IN EUROPE^{3,10}

Continuous apomorphine infusion has been used by clinicians in Europe to help deliver more consistent control of motor fluctuations for thousands of patients

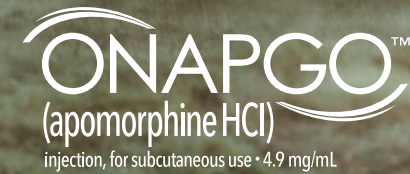
IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Serious Adverse Reactions After Intravenous Administration: Subcutaneous use only; thrombus formation and pulmonary embolism have followed intravenous administration.

Nausea and Vomiting: ONAPGO is known to cause nausea and vomiting (may be severe) when administered at recommended doses. Antiemetics with anti-dopaminergic actions have the potential to worsen PD symptoms. Consider starting therapy, without antiemetics, at 1 mg and titrate based upon effectiveness and tolerance.

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



EXPLORE THE ONAPGO ROUTE

- 

UNAFFECTED BY GI DYSMOTILITY

Continuous apomorphine infusion bypasses the GI tract, avoiding GI and food issues^{1,6,11,12}
- 

PREDICTABLE CNS UPTAKE

Apomorphine does not have protein competition for entry to the brain and no metabolic conversion needed^{1,11,12}
- 

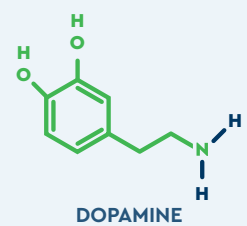
DIRECT POSTSYNAPTIC RECEPTOR STIMULATION

Apomorphine overcomes the loss of buffering capacity and fluctuating dopamine concentrations by acting directly on postsynaptic dopamine receptors^{1,13}

APOMORPHINE IS STRUCTURALLY SIMILAR TO DOPAMINE^{1,12,13}

It has dopamine-like stimulation of the D1-receptor and a balanced affinity for the D2-family receptors.

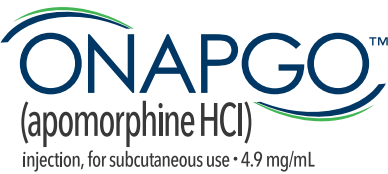
The precise mechanism of action of ONAPGO is unknown.¹



IMPORTANT SAFETY INFORMATION (cont'd) WARNINGS AND PRECAUTIONS (cont'd)

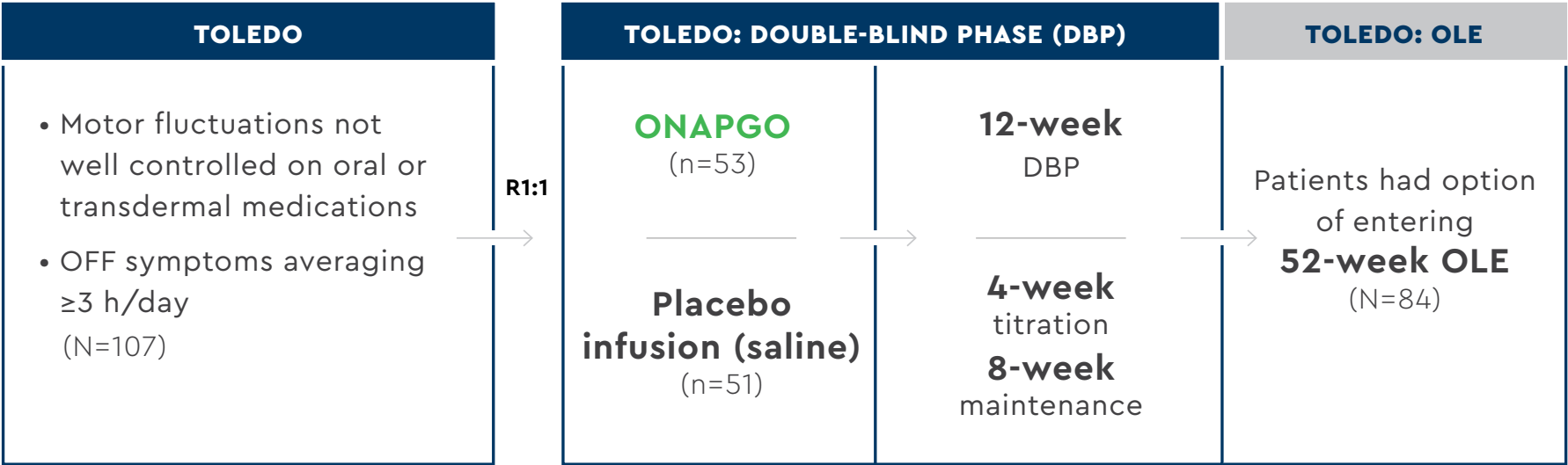
Falling Asleep During Activities of Daily Living (ADL) and Somnolence: Somnolence is commonly associated with ONAPGO. Before initiating treatment, advise patients of risk and assess for factors that can increase it. If significant daytime sleepiness develops or patients fall asleep during ADL, ONAPGO should ordinarily be stopped. If continued, advise patients not to drive and avoid other potentially dangerous activities. There is insufficient information to determine if dose reduction will eliminate episodes of falling asleep during ADL.

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Pivotal trial and open-label extension

A Phase 3, 12-week, multicenter, parallel-group, double-blind, randomized, placebo-controlled study in Europe evaluated the efficacy and safety of ONAPGO, followed by a 52-week open-label extension (OLE).^{1,9,14}



Patients had the option to switch early into the open-label phase due to lack of efficacy.

ASSESSED FROM BASELINE TO 12 WEEKS:

PRIMARY ENDPOINT¹

- Mean change in total daily OFF time

KEY SECONDARY ENDPOINTS^{1,14}

- Mean change in daily GOOD ON time*
- Patient Global Impression of Change (PGI-C)

OTHER SECONDARY ENDPOINTS¹⁴

- Mean change in oral levodopa (LD) dose
- Mean change in levodopa-equivalent dose (LED)

TOLEDO OLE study limitations¹⁰:

Open-label study design including lack of comparator arm, decreasing sample size, and potential continued involvement of responders and attrition of nonresponders; no sample size estimations (100 subjects considered adequate to meet the objectives); all analyses performed descriptively; and no hypothesis testing, therefore no testing for multiple comparisons.

*GOOD ON time=ON time without troublesome dyskinesia.

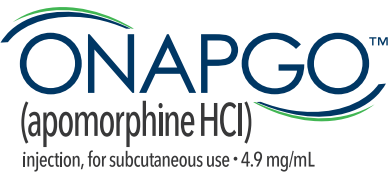
Please see [page 8](#) for dosing and titration.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

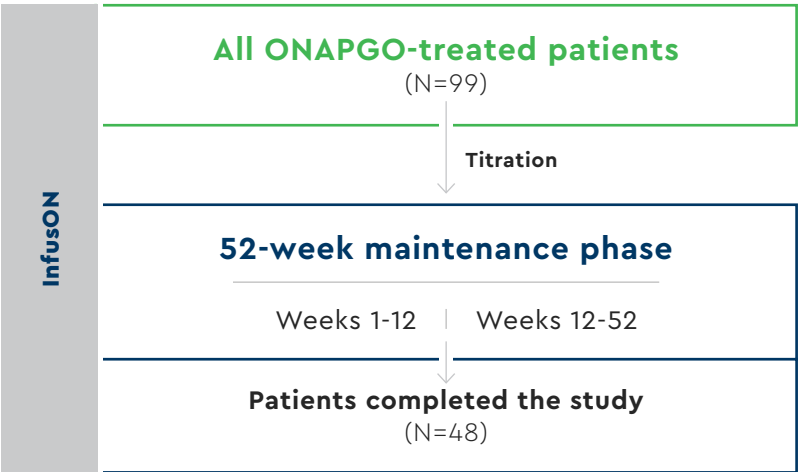
Syncope/Hypotension/Orthostatic Hypotension: ONAPGO may cause orthostatic hypotension at any time, but especially during dose escalation. Patients should avoid alcohol when using ONAPGO and lie down before and after taking sublingual nitroglycerin. Other vasodilators and antihypertensives may also increase hypotensive effects. Monitor blood pressure in patients taking concomitant antihypertensive medications or vasodilators.

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



Confirmatory US open-label trial

A Phase 3, multicenter, open-label study of ONAPGO in patients with PD in the US.¹⁵



ASSESSED FROM BASELINE TO 12 WEEKS:

PRIMARY ENDPOINT¹⁵

- Mean change in daily OFF time

KEY SECONDARY ENDPOINTS¹⁵

- Mean change in daily GOOD ON time*
- PGI-C
- Mean change in LD dose and LED

InfusON study limitations^{10,15}:

Open-label study design including lack of comparator arm, decreasing sample size and potential continued involvement of responders and attrition of nonresponders; no sample size estimation (up to 100 subjects considered adequate to meet the objectives); all analyses performed descriptively; and no hypothesis testing, therefore no testing for multiple comparisons.

Please see [page 8](#) for dosing and titration.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Falls: Patients with PD are at risk of falling due to underlying postural instability, possible autonomic instability, and syncope caused by blood pressure lowering effects of PD drugs. ONAPGO may increase risk of falling by simultaneously lowering blood pressure and altering mobility.

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Baseline characteristics were balanced across all studies^{1,10,14,15}

Select Baseline Characteristics (full analysis set)	TOLEDO [†]		InfusON [‡]
	ONAPGO (n=53)	PLACEBO (n=51)	ONAPGO (N=99)
Age, years (range)	63.6 (42-80)	63.0 (41-78)	61.6 (32-83)
Disease duration, years (SD)	11.9	10.8	10.0 (6.22)
OFF time, h/day (range)	6.7 (3.0-12.5)	6.8 (2.3-15.3)	6.6 (2.2-14.0)
GOOD ON, h/day	8.6	8.6	9.3
Taking LD-containing drug, %	100	100	100
Daily LD dose, mg (range)	920.4 (200.0–2800.0)	989.0 (175.0–2150.0)	1068.0 (100.0-3150.0)
Daily LED, mg (range)	1485.5 (465.0–3790.0)	1472.6 (580.0–2842.5)	1441.8 (240.0-3850.0)
Antiparkinsonian adjunctive therapy			
Dopamine agonist, %	91	79	80
COMT inhibitor, %	60	62	20
MAO-B inhibitor, %	43	38	33
Amantadine, %	30	23	31
At baseline in TOLEDO, in addition to LD ¹⁰ :			
95% were taking ≥1 concomitant PD medication		Despite adjustments, patients still had ≥3 HOURS OF DAILY OFF TIME. ¹	
74% were taking ≥2 concomitant PD medications			

*GOOD ON time=ON time without troublesome dyskinesia.
[†]TOLEDO values are listed from the following sources in this order: ONAPGO USPI (modified intention-to-treat [mITT]); Katzenschlager et al, 2018 (full analysis set); Data on file (mITT).^{1,10,14}
[‡]All InfusON values are from the safety population except OFF range, GOOD ON range, and LD and LED doses, which are from the mITT population (n=94).¹⁵



TOLEDO: Dosing and Titration^{1,9,10,14}

ONAPGO or placebo infusion was initiated at 1 mg/h over 5-10 days (based on tolerability) in hospital or outpatient setting. Subjects were titrated to achieve efficacy and tolerability (at visits up to Week 4) by adjusting the dosage by 0.5 to 1 mg/h daily or weekly to a maximum continuous dosage of 8 mg/h. The mean final continuous dosage was 4.68 mg/h (SD 1.50) in the ONAPGO group vs 5.76 mg/h (SD 1.79) in the placebo group.* Use of the bolus function of the device was not permitted. Antiemetic premedication was administered according to local practice. Domperidone was recommended at 10 mg 3 times a day, starting 3 days before the first infusion.

At baseline, patients had >6 hours of OFF time. Patients in both treatment groups remained on concomitant oral PD medications throughout trial. Reductions in concomitant PD medications during the titration period were driven by the emergence of dopaminergic effects, including dyskinesia. Dose reductions were made in the following order: dopamine agonists, MAO-B inhibitors, COMT inhibitors, levodopa.

TOLEDO OPEN-LABEL EXTENSION

All patients were retitrated starting at 1 mg/h until optimal rate over 1-3 days (based on tolerability and efficacy). Subjects were titrated to a target range of 3-8 mg/h over 16 h/day (±2 h). The mean continuous dosage was 4.45 mg/h (SD 1.41) for patients previously on ONAPGO and 4.71 mg/h (SD 1.73) for ONAPGO-naïve patients. Use of the bolus doses was permitted.

*The mean continuous infusion rate across studies, as stated in the ONAPGO USPI, was 4 mg/h; also stated in the USPI, the maximum dosing rate is 6 mg/h.

InfusON: Dosing and Titration^{10,15}

The initiation/titration period was 4 to 51 days. Patients were initiated with an extra+ (bolus) dose of ONAPGO 1 to 2 mg followed by an infusion rate starting at 1 mg/h and titrated by 0.5 to 1 mg/h as needed to achieve efficacy and tolerability (maximum 8 mg/h; over 16 h/day), at which point the patient entered the maintenance phase. The mean continuous dosage after titration was 3.8 mg/h (SD 1.41). Antiemetic treatment with trimethobenzamide 300 mg 3 times daily was permitted, starting 2 to 3 days before ONAPGO titration, and up to 12 weeks as needed. Up to three 2 mg bolus doses per day were permitted.

Oral dose reduction of dopamine agonists, MAO-B inhibitors, COMT inhibitors, and LD was driven by occurrence of dopaminergic adverse events and troublesome dyskinesia; dopamine agonists were reduced first.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Infusion Site Reactions and Infections: Reactions have been reported including nodules, erythema, hematomas, inflammation, pruritus, swelling, discoloration, hemorrhage, hypersensitivity, induration, edema, pain, rash, or bruising. If an infection is suspected, such as cellulitis, which was reported, the cannula should be removed from the infusion site and a new cannula placed at a new infusion site. In the event of a prolonged interruption of treatment with ONAPGO, the patient should be prescribed oral medications to treat their PD.

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).

TOLEDO



Significant reduction in daily OFF time accompanied by a similar significant increase in GOOD ON time at 12 weeks¹

TOLEDO: DBP

↓

LESS OFF TIME¹

-2.6 h/day

vs

-0.9 h/day placebo

(primary endpoint)

(P=0.0114)

↑

MORE GOOD ON TIME¹

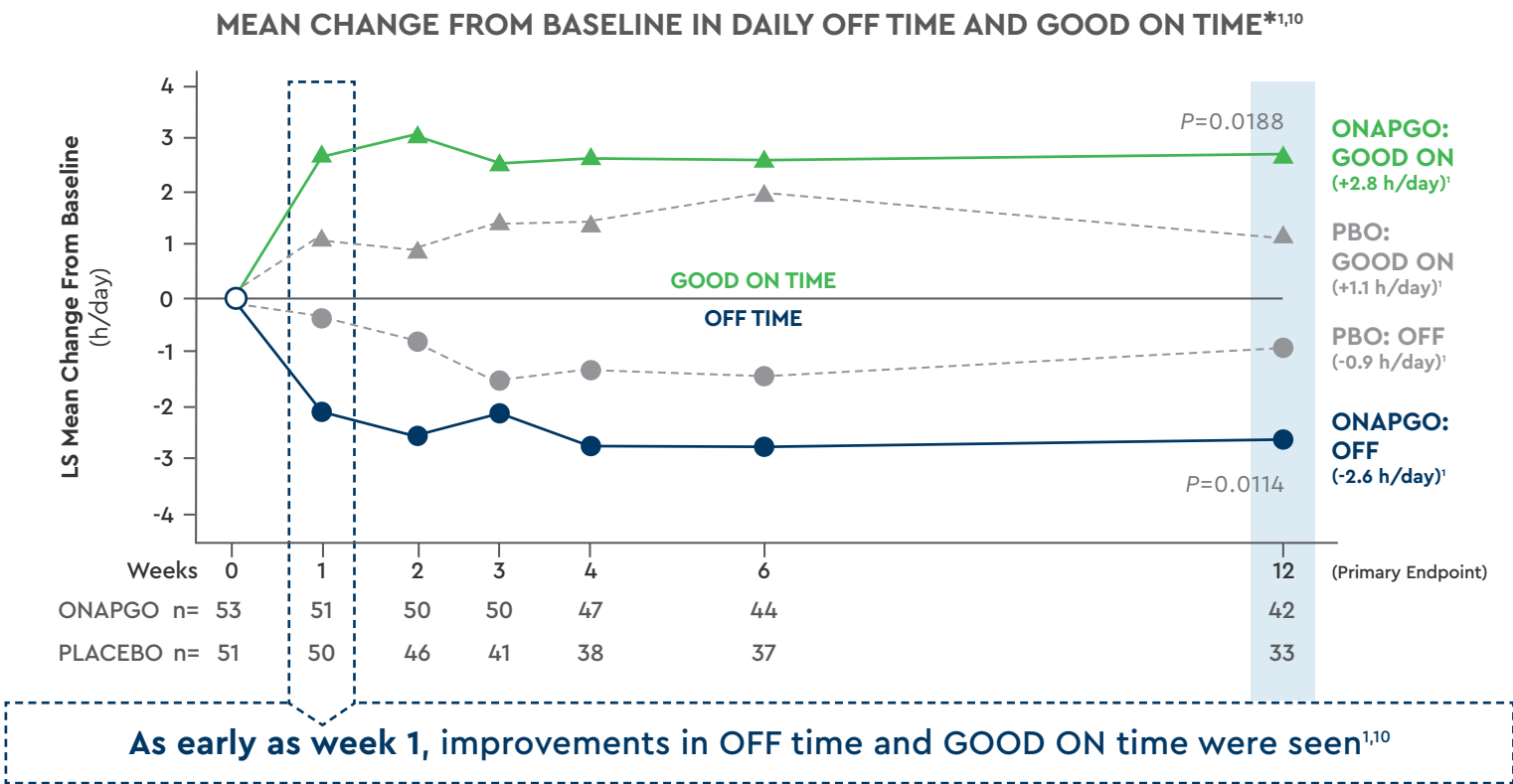
+2.8 h/day

vs

+1.1 h/day placebo

(key secondary endpoint)

(P=0.0188)



PATIENT IMPACT (PGI-C)¹

More ONAPGO-treated patients reported improvement in general health vs placebo at Week 12

(key secondary endpoint; P<0.0001)¹⁰

79% ONAPGO (n=43)

24% Placebo (n=34)

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

Hallucinations/Psychotic-Like Behavior: Patients with a major psychotic disorder should ordinarily not be treated with ONAPGO due to risk of exacerbating psychosis. Also, certain medications used to treat psychosis may exacerbate symptoms of PD and decrease effectiveness of ONAPGO.

Dyskinesia: ONAPGO may cause dyskinesia or exacerbate pre-existing dyskinesia.

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).

TOLEDO



TOLEDO safety¹

Adverse reactions (ARs) reported by ≥5% of patients receiving ONAPGO and higher than placebo in TOLEDO DBP.¹

ADVERSE REACTIONS	ONAPGO* (%), n=54	PLACEBO (%), n=53
Infusion site nodule	44	0
Nausea	22	9
Somnolence	22	4
Infusion site erythema	17	4
Dyskinesia	15	0
Headache	13	4
Insomnia	11	2
Dizziness	9	4
Hypotension	7	0
Asthenia	7	0
Fatigue	7	2
Constipation	7	6
Vomiting	7	4

*Variable doses.¹

[†]1 patient discontinued for each of the following: nausea, orthostatic intolerance, visual hallucination, gait disturbance, infusion site nodule, and hypotension.¹

TOLEDO OLE: Consistent safety profile across all newly treated ONAPGO patients in the open-label extension. No new safety signals were observed. 4 patients in the double-blind group and 10 patients in the ONAPGO-naïve group discontinued due to ARs.^{1,9,10}

Infusion site nodule formation and erythema were generally mild to moderate¹⁴

Rate of hallucinations:
4% ONAPGO vs 4% placebo¹

Discontinuation rates

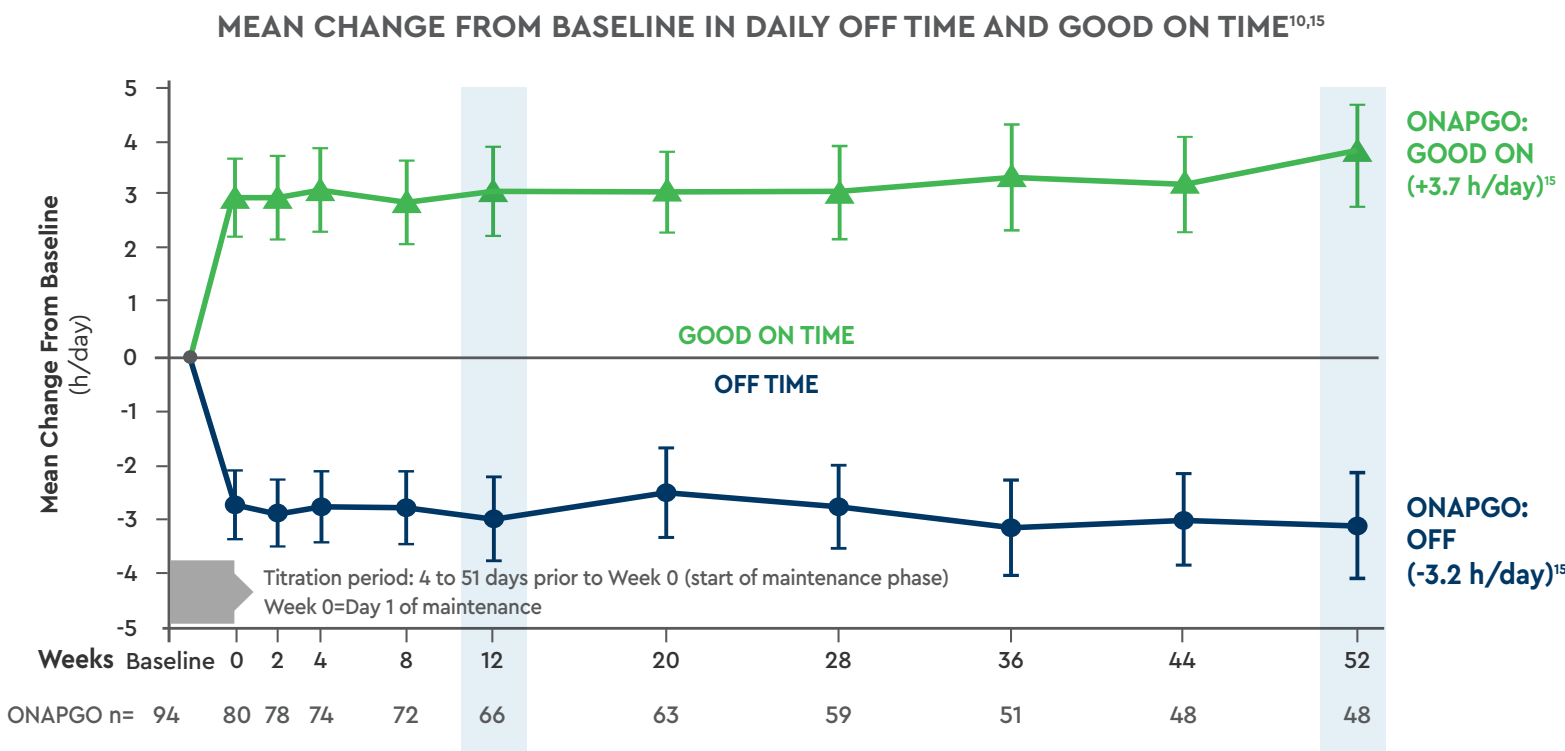
6 patients (11%) receiving ONAPGO vs none receiving placebo discontinued due to ARs^{†1}

- No consistent pattern of ARs or dose relationship for study discontinuation found¹⁰
- None due to dyskinesia¹

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



Improvements in motor fluctuations sustained through 52 weeks in US-based open-label study^{10,15}



InfusON results consistent with TOLEDO^{1,9,15}

LESS OFF TIME

-3.0 h/day
Through 12 weeks (primary endpoint)

-3.2 h/day
Through 52 weeks

MORE GOOD ON TIME

+3.1 h/day
Through 12 weeks (key secondary endpoint)

+3.7 h/day
Through 52 weeks

PATIENT IMPACT (PGI-C)¹⁵

ONAPGO patients reported **improvement in general health** at Weeks 12 and 52

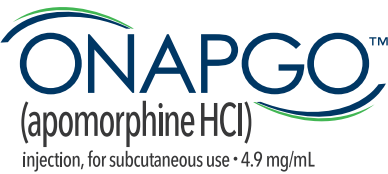
89%
Week 12 (n=75)
(key secondary endpoint)

90%
Week 52 (n=49)

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

Hemolytic Anemia: Hemolytic anemia requiring hospitalization has been reported. Many cases included positive Coombs test. Severe anemia, angina, and dyspnea have occurred. Some patients were treated with high-dose glucocorticoids or blood transfusions. It can occur at any time after treatment. If a patient develops anemia while taking ONAPGO, consider a hemolytic anemia workup; if it occurs, consider stopping treatment.

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



InfusON safety profile consistent with TOLEDO¹⁵

Treatment-related ARs ≥5% after titration and at 52 weeks.**

Preferred Term, %	Titration Period (%) (N=99)	Maintenance Period Through Week 52 (%) (N=85)	Overall (%) (N=99)
Infusion site nodule	62	44	78
Dyskinesia	28	18	38
Infusion site erythema	20	13	27
Nausea	23	9	29
Somnolence	16	12	25
Dizziness	15	8	20
Headache	9	6	14
Infusion site pruritus	8	7	13
Fatigue	5	8	12
Infusion site bruising	8	5	12
Infusion site pain	6	5	10
Fall	4	8	10
Anxiety	4	4	7
Insomnia	3	4	6
Vomiting	3	4	5
Hallucination	1	5	5
Dyspnea	2	4	5
Hypotension	2	4	5
Orthostatic hypotension	4	1	5

MOST REACTIONS WERE MILD OR MODERATE¹⁵

- 17 patients discontinued during the titration phase; 16 discontinued during the maintenance phase
- 11 patients reported adverse events potentially suggestive of impulse control disorders, 9 (82%) were using concomitant dopamine agonists
- 5 patients reported hallucinations throughout the 52-week study (1 during titration and 4 during maintenance)

*Safety population.

*Adverse events are assigned to titration or maintenance periods based on date of onset. Because a patient may report an adverse event that appears in the Titration Period column and again in the Maintenance Period column, the values in those columns may not sum to the value in the Overall column.

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



Start their day with ON-SNAP-GO



1 cartridge per day¹
Prefilled and ready to use

Stored at room temperature¹
68-77 °F (20-25 °C); no refrigeration required

Reversible, all-day infusion (e.g., 16 h)^{1,9}
Added on to existing oral regimen at start

No surgery required^{1,9}

Prior to use, patients and care partners should receive education about the ONAPGO device as detailed in the Instructions for Use.^{1,16}

“ Now ONAPGO is just another part of my daily routine. After training, setup takes me less than 5 minutes each day. ”

—JOE, 61, real person on ONAPGO

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)
Impulse Control/Compulsive Behaviors: Patients may experience intense urges and inability to control them while taking ONAPGO. Because patients may not recognize these behaviors as abnormal, it is important to specifically ask about new or increased urges with ONAPGO. Consider dose reduction or stopping medication if urges develop.

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Continuous patient support

The ONAPGO Circle of Care™ program surrounds patients and care partners with a team of experts who provide support from the moment ONAPGO is prescribed.



HUB COORDINATORS

Assigned to each patient to assist with:

- Understanding patient insurance coverage, benefits, and available assistance programs
 - Access support services including benefits investigation, prior authorization, and appeal assistance
 - Specialty pharmacy coordination
- » Field Access Specialists available for clinician offices to help support and guide patient access

CLINICAL NURSE NAVIGATORS

Experienced registered nurses who provide high-touch, personalized patient and care partner support including:

- Starting and titrating ONAPGO in-home*
- In-home training and education, including skin management, wearing and using the device, as well as ongoing education for their entire time on ONAPGO
- Collaboration and communication with the clinician's office



» Device training, education, and in-services are also available to clinicians and their office teams.

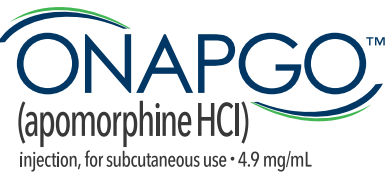
*Or in-office if indicated on the prescription and enrollment form.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Cardiac Events: ONAPGO can reduce resting systolic and diastolic blood pressure and may have potential to exacerbate cardiac (and cerebral) ischemia in patients with known cardiovascular and cerebrovascular disease. If patients develop signs and symptoms of cardiac or cerebral ischemia, re-evaluate continued ONAPGO use.

Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).

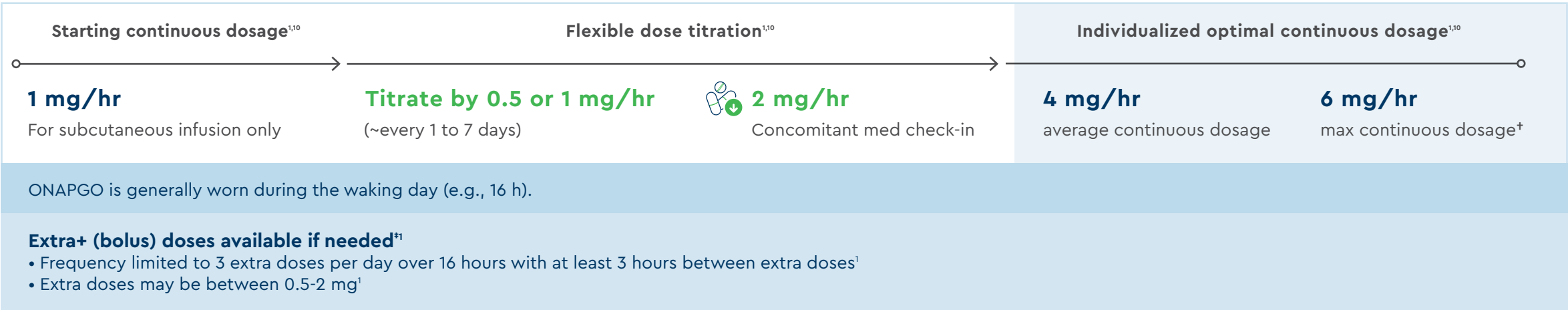


Starting patients on ONAPGO

Submit Prescription and Enrollment Form, signed by patient and clinician

- HUB conducts benefits investigation
- Patient receives welcome call from **Clinical Nurse Navigator** to set up in-home training and education visits
- Clinician's office submits **prior authorization**

Each patient's dose should be titrated to optimal effectiveness and tolerability.*¹



*ONAPGO should be started and titrated under medical supervision to ensure training and monitoring for potential side effects.¹

[†]The maximum recommended daily dose, including extra doses, is 98 mg during the waking day (e.g., 16 h).¹

[‡]Extra+ (bolus) doses may be used upon starting in the morning or restarting the continuous dose after a 1-hour or longer break in use. Can also be used as a supplement to the continuous dosage to manage acute OFF symptoms not controlled.¹

Renal impairment considerations: mild or moderate renal impairment initial extra dose: 0.5-1 mg (should not exceed 1 mg); no adjustment for subsequent extra doses.¹

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

QTc Prolongation and Potential for Proarrhythmic Effects: There is a dose-related prolongation of QTc interval after apomorphine exposure similar to that achieved with therapeutic doses of ONAPGO. Drugs that prolong QTc have been associated with torsades de pointes and sudden death. Consider risks and benefits of ONAPGO treatment prior to initiating in patients with risk factors for prolonged QTc.

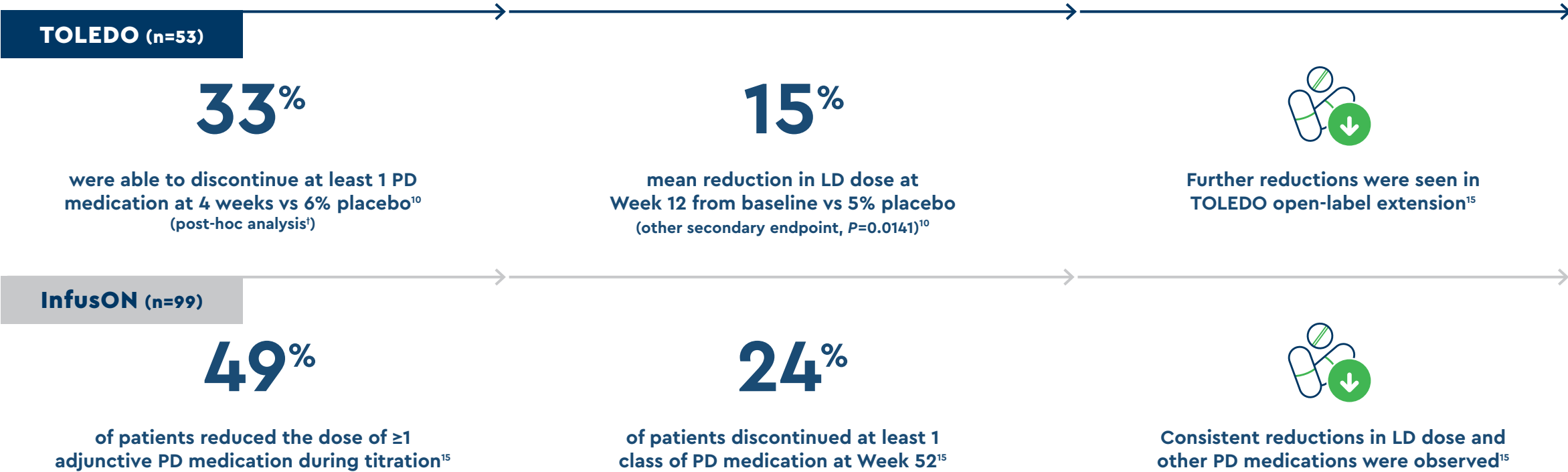
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Concomitant PD medication reduction

In clinical trials, patients on ONAPGO were able to reduce or discontinue concomitant medications^{*1,9,10}

» Adjustments may be needed during titration—generally seen around the 2 mg/hr dose; check in with your patient during this time.^{1,10}
In clinical trials, the order of medication reduction was as follows: dopamine agonists first, followed by either MAO-B inhibitors, COMT inhibitors, and/or LD.^{14,15}



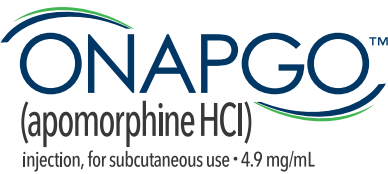
^{*}All patients treated with ONAPGO in the double-blind study were maintained on levodopa.¹
[†]Post-hoc analysis results should be interpreted with caution since findings are not pre-specified and may be exploratory in nature, without adjustment for multiple comparisons. Data are descriptive and conclusions cannot be drawn.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hypersensitivity: Allergic reactions like urticaria, rash, pruritus, and/or manifestations of angioedema may occur due to ONAPGO or its sulfite excipient sodium metabisulfite, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes. Sulfite sensitivity prevalence is unknown, probably low, and seen more frequently in asthmatic people.

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IMPORTANT SAFETY INFORMATION

INDICATION

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IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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ONAPGO is contraindicated in patients who have demonstrated hypersensitivity/allergic/anaphylactic reaction to it or any of its excipients, including sulfite (i.e., sodium metabisulfite).

WARNINGS AND PRECAUTIONS

Serious Adverse Reactions After Intravenous Administration: Subcutaneous use only; thrombus formation and pulmonary embolism have followed intravenous administration.

Nausea and Vomiting: ONAPGO is known to cause nausea and vomiting (may be severe) when administered at recommended doses. Antiemetics with anti-dopaminergic actions have the potential to worsen PD symptoms. Consider starting therapy, without antiemetics, at 1 mg and titrate based upon effectiveness and tolerance.

Falling Asleep During Activities of Daily Living (ADL) and Somnolence: Somnolence is commonly associated with ONAPGO. Before initiating treatment, advise patients of risk and assess for factors that can increase it. If significant daytime sleepiness develops or patients fall asleep during ADL, ONAPGO should ordinarily be stopped. If continued, advise patients not to drive and avoid other potentially dangerous activities. There is insufficient information to determine if dose reduction will eliminate episodes of falling asleep during ADL.

Syncope/Hypotension/Orthostatic Hypotension: ONAPGO may cause orthostatic hypotension at any time, but especially during dose escalation. Patients should avoid alcohol when using ONAPGO and lie down before and after taking sublingual nitroglycerin. Other vasodilators and antihypertensives may also increase hypotensive effects. Monitor blood pressure in patients taking concomitant antihypertensive medications or vasodilators.

Falls: Patients with PD are at risk of falling due to underlying postural instability, possible autonomic instability, and syncope caused by blood pressure lowering effects of PD drugs. ONAPGO may increase risk of falling by simultaneously lowering blood pressure and altering mobility.

Infusion Site Reactions and Infections: Reactions have been reported including nodules, erythema, hematomas, inflammation, pruritus, swelling, discoloration, hemorrhage, hypersensitivity, induration, edema, pain, rash, or bruising. If an infection is suspected, such as cellulitis, which was reported, the cannula should be removed from the infusion site and a new cannula placed at a new infusion site. In the event of a prolonged interruption of treatment with ONAPGO, the patient should be prescribed oral medications to treat their PD.

Hallucinations/Psychotic-Like Behavior: Patients with a major psychotic disorder should ordinarily not be treated with ONAPGO due to risk of exacerbating psychosis. Also, certain medications used to treat psychosis may exacerbate symptoms of PD and decrease effectiveness of ONAPGO.

Dyskinesia: ONAPGO may cause dyskinesia or exacerbate pre-existing dyskinesia.

Hemolytic Anemia: Hemolytic anemia requiring hospitalization has been reported. Many cases included positive Coombs test. Severe anemia, angina, and dyspnea have occurred. Some patients were treated with high-dose glucocorticoids or blood transfusions. It can occur at any time after treatment. If a patient develops anemia while taking ONAPGO, consider a hemolytic anemia workup; if it occurs, consider stopping treatment.



IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Impulse Control/Compulsive Behaviors: Patients may experience intense urges and inability to control them while taking ONAPGO. Because patients may not recognize these behaviors as abnormal, it is important to specifically ask about new or increased urges with ONAPGO. Consider dose reduction or stopping medication if urges develop.

Cardiac Events: ONAPGO can reduce resting systolic and diastolic blood pressure and may have potential to exacerbate cardiac (and cerebral) ischemia in patients with known cardiovascular and cerebrovascular disease. If patients develop signs and symptoms of cardiac or cerebral ischemia, re-evaluate continued ONAPGO use.

QTc Prolongation and Potential for Proarrhythmic Effects: There is a dose-related prolongation of QTc interval after apomorphine exposure similar to that achieved with therapeutic doses of ONAPGO. Drugs that prolong QTc have been associated with torsades de pointes and sudden death. Consider risks and benefits of ONAPGO treatment prior to initiating in patients with risk factors for prolonged QTc.

Hypersensitivity: Allergic reactions like urticaria, rash, pruritus, and/or manifestations of angioedema may occur due to ONAPGO or its sulfite excipient sodium metabisulfite, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes. Sulfite sensitivity prevalence is unknown, probably low, and seen more frequently in asthmatic people.

Fibrotic Complications: Retroperitoneal fibrosis, pulmonary infiltrates, pleural effusion, pleural thickening, and cardiac valvulopathy have been reported with ergot-derived dopaminergic agents. Complete resolution does not always occur when drug is stopped. Reactions are believed to be related to ergoline structure. It's unknown whether non-ergot derived dopamine agonists, such as ONAPGO, can cause these reactions.

Priapism: In clinical studies of intermittent apomorphine injection, painful erections were reported in 3 of 361 men treated with intermittent subcutaneous injection, and one patient withdrew from therapy because of priapism; although no patients in the clinical studies required surgical intervention, severe priapism may require surgical intervention.

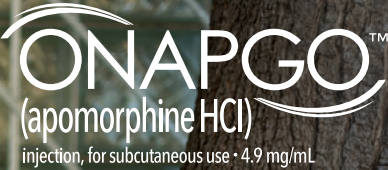
ADVERSE REACTIONS

Most common adverse reactions (incidence ≥10% on ONAPGO and at least twice the rate of placebo) were infusion site nodule, nausea, somnolence, infusion site erythema, dyskinesia, headache, and insomnia.

Please see full [Prescribing Information](#).

References: **1.** ONAPGO. Package insert. Supernus Pharmaceuticals, Inc. **2.** Tanner CM. Exploring the clinical burden of OFF periods in Parkinson disease. *Am J Manag Care.* 2020;26(suppl 12):S255-S264. **3.** Trenkwalder C, Chaudhuri KR, Garcia Ruiz PJ, et al. Expert Consensus Group report on the use of apomorphine in the treatment of Parkinson's disease—clinical practice recommendations. *Parkinsonism Relat Disord.* 2015;21(9):1023-1030. **4.** Kuhl M. Capturing and elevating the patient voice. The Michael J. Fox Foundation for Parkinson's Research. November 10, 2014. Accessed March 7, 2024. <https://www.michaeljfox.org/foundation/news-detail.php?capturing-and-elevating-the-patient-voice> **5.** Schapira AH, Emre M, Jenner P, Poewe W. Levodopa in the treatment of Parkinson's disease. *Eur J Neurol.* 2009;16(9):982-989. **6.** Pfeiffer RF, Isaacson SH, Pahwa R. Clinical implications of gastric complications on levodopa treatment in Parkinson's disease. *Parkinsonism Relat Disord.* 2020;76:63-71. **7.** Tambasco N, Romoli M, Calabresi P. Levodopa in Parkinson's disease: current status and future developments. *Curr Neuroparmacol.* 2018;16(8):1239-1252. **8.** Leta V, Klingelhoefer L, Longardner K, et al. Gastrointestinal barriers to levodopa transport and absorption in Parkinson's disease. *Eur J Neurol.* 2023;30(5):1465-1480. **9.** Katzenschlager R, Poewe W, Rascol O, et al. Long-term safety and efficacy of apomorphine infusion in Parkinson's disease patients with persistent motor fluctuations: results of the open-label phase of the TOLEDO study. *Parkinsonism Relat Disord.* 2021;83:79-85. **10.** Data on file. Supernus Pharmaceuticals, Inc. **11.** Oebering CD, Chen JJ, Swope DM. Update on apomorphine for the rapid treatment of hypomobility ("off") episodes in Parkinson's disease. *Pharmacotherapy.* 2006;26(6):840-852. **12.** Jenner P, Katzenschlager R. Apomorphine—pharmacological properties and clinical trials in Parkinson's disease. *Parkinsonism Relat Disord.* 2016;33(suppl 1):S13-S21. **13.** Torti M, Bravi D, Vacca L, Stocchi F. Are all dopamine agonists essentially the same? *Drugs.* 2019;79(7):693-703. **14.** Katzenschlager R, Poewe W, Rascol O, et al. Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial. *Lancet Neurol.* 2018;17(9):749-759. **15.** Isaacson SH, Espay AJ, Pahwa R, et al. Continuous, subcutaneous apomorphine infusion for Parkinson disease motor fluctuations: results from the phase 3, long-term, open-label United States InfusON study. *J Parkinsons Dis.* 2025;15(2):361-373. **16.** ONAPGO. Instructions for Use. Supernus Pharmaceuticals, Inc. **17.** Isaacson SH, Grall MS, Gupta F, et al. Protocol to help neurologists manage subcutaneous apomorphine therapy skin nodules: expert roundtable recommendations. Poster presented at: International Association for Parkinsonism and Related Disorders (IAPRD) Congress; May 13–16, 2023; Chicago, IL.

MORE ONAPGO™ TIME



CONTINUOUS TREATMENT

All-day subcutaneous infusion, added on to existing regimens, and worn during the waking day (e.g., 16 h)^{1,14}

CONSISTENT CONTROL

Significant reduction in daily OFF time accompanied by a significant increase in GOOD ON time¹

A DIFFERENT ROUTE

Apomorphine acts directly to help achieve more continuous, predictable daily control of motor fluctuations^{1,13}



Consider ONAPGO for patients in your practice:

Struggling with motor fluctuations despite increases and adjustments to CD/LD and adjunct oral medication(s)^{1,3}

Experiencing 3 or more hours of daily OFF time¹

As intermediate treatment before DBS or adjunctively post DBS^{3,15}

INDICATION

ONAPGO is indicated for the treatment of motor fluctuations in adults with advanced Parkinson's Disease (PD).

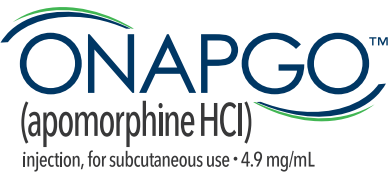
IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Concomitant use of ONAPGO with 5HT₃ antagonists is contraindicated based on reports of profound hypotension and loss of consciousness when ONAPGO was administered with ondansetron.

ONAPGO is contraindicated in patients who have demonstrated hypersensitivity/allergic/anaphylactic reaction to it or any of its excipients, including sulfite (i.e., sodium metabisulfite).

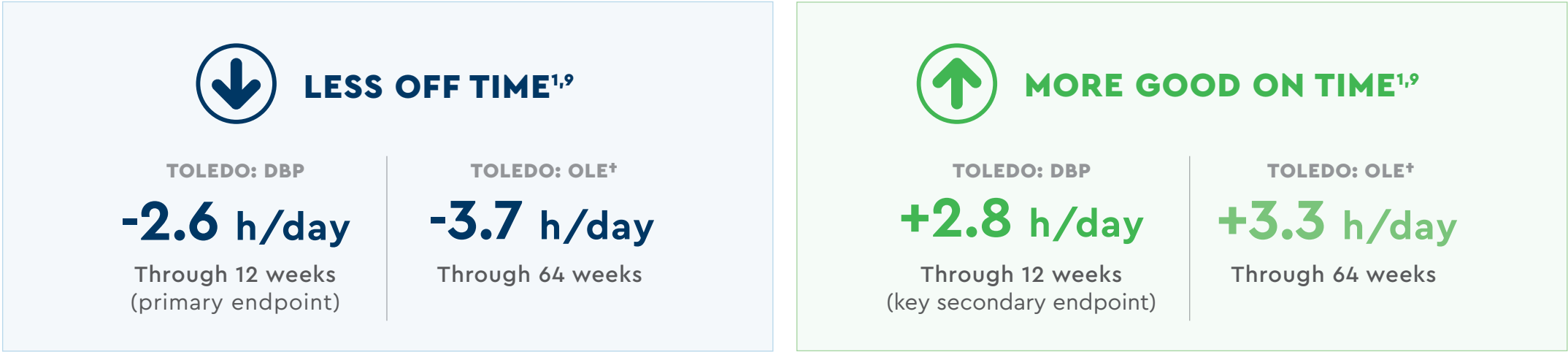
Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



Improvements in motor fluctuations sustained

Patients saw significant improvements throughout the 52-week open-label extension.*^{1,9}

ALL ONAPGO-TREATED PATIENTS THROUGH WEEK 64 (N=59[†])



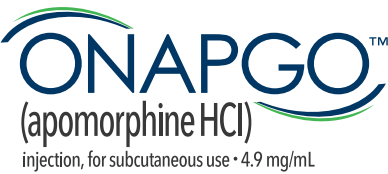
At the end of the open-label extension:



*All analyses for the open-label extension were conducted on the safety population.⁹
[†]59 patients completed the OLE study.⁹
[‡]Assumes a 16-hour waking day.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS

Serious Adverse Reactions After Intravenous Administration: Subcutaneous use only; thrombus formation and pulmonary embolism have followed intravenous administration.
Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).



Proper infusion site care

In clinical trials, infusion site reactions with ONAPGO^{1,10,15}:

| Were common, but usually mild to moderate* | May be more common early in therapy | Rarely led to discontinuation | Infusion site infections were uncommon

*Nodules were typically asymptomatic and generally resolved on their own over time.

Circle of Care™ Clinical Nurse Navigators will provide robust patient and care partner education and support on skin care management for the entire course of treatment.^{1,16,17}

1 SITE ROTATION

»

2 SKIN HYGIENE

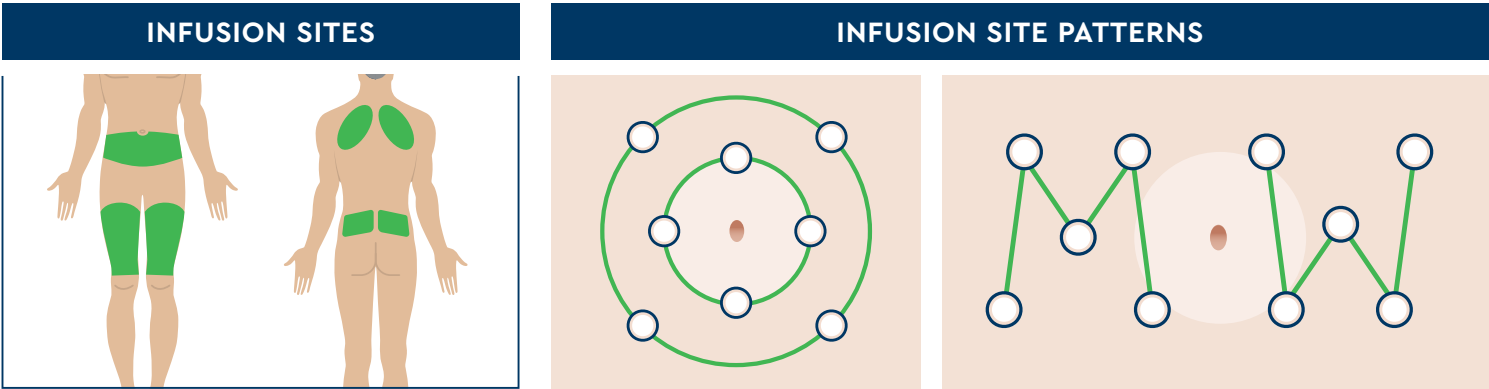
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3 PROPER INSERTION TECHNIQUE

»

4 CLEANING RESIDUAL MEDICATION FROM SKIN AFTER REMOVAL

INFUSION SITE PLACEMENT¹⁶
 Patients should choose an infusion site and rotate cannula placement daily, using an "O"- or "MW"-shaped pattern (at least 2 inches apart).



Please see additional Important Safety Information throughout and on [pages 17-18](#), and full [Prescribing Information](#).

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