I. OVERVIEW OF IN-CENTER NOCTURNAL HEMODIALYSIS

In-center nocturnal hemodialysis (INHD) is a hybrid home modality administered at a dialysis facility at night for six to eight hours, typically beginning between 5 p.m. and 9 p.m., three times per week. The longer, gentler treatment times that distinguish INHD are critical to the modality’s clinical and lifestyle benefits.

With a nocturnal program, a center can attract and retain working patients, increase capacity, and improve overall clinical outcomes and quality of life (QOL). The therapy is always selected by patients in consultation with their physicians and pursuant to their physicians’ orders. While INHD offers considerable clinical and lifestyle benefits, it may not be appropriate for all patients.

II. CLINICAL BENEFITS

Most reports on INHD are observational in nature; nevertheless, there are several consistent findings that highlight its clinical benefits. Lacson et al.1 summarized a cohort study on 746 INHD patients matched to 2,062 in-center hemodialysis (ICHD) patients by propensity score, geographic area, and incident patient status. One-year mortality rates were 9% for INHD and 15% for ICHD, and two-year mortality rates were 19% and 27%, respectively. This represents a 27% relative risk reduction by the first year and a 25% relative risk reduction by the second year with INHD. The mean Kt/V for patients who converted from ICHD to INHD increased from 1.4 to 2.3, while the mean ultrafiltration rate (UFR) decreased 45%—from 11 mL/kg/hr to 6 mL/kg/hr. Among laboratory parameters, phosphorus decreased from 5.73 mg/dL to 5.02 mg/dL (P < 0.001). There were no statistically significant differences in albumin and hemoglobin levels in INHD versus ICHD patients.

In addition, a prospective trial reported by Ok et al\(^2\) matched 247 INHD patients and 247 period-prevalent ICHD patients based on age, gender and the presence of diabetes, and noted a 72% relative mortality risk reduction in the INHD cohort over an average follow-up of 11.3 months.

Jakubovic et al\(^3\) reviewed world-wide experiences with INHD and the associated literature (22 total studies), focusing on hospitalization rates, cardiovascular remodeling, volume and blood pressure (BP) control, phosphate and mineral metabolism, anemia, sleep abnormalities and overall QOL. The studies indicated that INHD is associated with fewer hospital days per 100 patient months, regressed left ventricular hypertrophy (LVH) and left atrial diameter, and improved ejection fraction—although this observation warrants further study.\(^4\) Patients demonstrated improved BP control, a reduced need for anti-hypertensive medications, and maintained hemoglobin levels with a mild decrease in ESA dosage patterns. INHD patients also demonstrated improved daytime function, oxygen desaturation index levels and sleep quality. They reported better QOL, heartier appetites, higher energy levels, fewer intra-dialytic cramps and shorter post-treatment recoveries. The main challenges for patients on INHD included sleeping difficulties in the dialysis center, with frequent interruptions by treatment safety monitoring protocols, such as checking BP.

### III. DAVITA IN-CENTER NOCTURNAL HEMODIALYSIS TODAY

Approximately 1% of DaVita patients utilize INHD at approximately 6% of DaVita hemodialysis facilities, which average 10 INHD patients per facility (excluding any ICHD patients who dialyze for standard four-hour treatments during the nocturnal shift).

**Prescribing INHD**

The table below summarizes how physicians currently prescribe INHD to DaVita patients:

<table>
<thead>
<tr>
<th>(April 2015)</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Time (min)</td>
<td>414</td>
<td>300</td>
<td>72</td>
</tr>
<tr>
<td>Dialysate Flow Rate (mL/min)</td>
<td>545</td>
<td>600</td>
<td>87</td>
</tr>
<tr>
<td>Blood Flow Rate (mL/min)</td>
<td>322</td>
<td>300</td>
<td>47</td>
</tr>
<tr>
<td>Bicarb Dialysate (mE q/L)</td>
<td>35.5</td>
<td>35.0</td>
<td>13.0</td>
</tr>
<tr>
<td>Heparin Bolus Load (units)</td>
<td>3,262</td>
<td>2,500</td>
<td>1,495</td>
</tr>
<tr>
<td>Heparin Infusion (units/hr)</td>
<td>988</td>
<td>1,000</td>
<td>515</td>
</tr>
</tbody>
</table>

\(^*\) Prescription data includes all in-center nocturnal patients with 8 or more treatments who had average MD orders > 6 hours in April 2015

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Superior clinical outcomes*

DaVita INHD clinical outcomes continue to be among the best of any modality, as illustrated in the table below:

<table>
<thead>
<tr>
<th>(April 2015)</th>
<th>INHD</th>
<th>ICHD</th>
<th>HHD</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequacy Kt/V ≥ 1.2</td>
<td>99%</td>
<td>98%</td>
<td>90%**</td>
<td>99%**</td>
</tr>
<tr>
<td>Albumin ≥ 3.5</td>
<td>93%</td>
<td>86%</td>
<td>92%</td>
<td>65%</td>
</tr>
<tr>
<td>Albumin ≥ 4.0</td>
<td>62%</td>
<td>45%</td>
<td>59%</td>
<td>22%</td>
</tr>
<tr>
<td>Phosphorus ≤ 5.5</td>
<td>72%</td>
<td>71%</td>
<td>67%</td>
<td>64%</td>
</tr>
<tr>
<td>PTH 150–600</td>
<td>64%</td>
<td>71%</td>
<td>56%</td>
<td>66%</td>
</tr>
<tr>
<td>URR ≥ 65</td>
<td>98%</td>
<td>97%</td>
<td>—</td>
<td>82%</td>
</tr>
</tbody>
</table>

* April 2015 clinical outcomes (Source: Nocturnal clinical model, LAB report, SMOR report, Snowi)
** Adequacy for HHD is Kt/V ≥ 2.0 and for PD is Kt/V ≥ 1.7

A word on treatment time

A small percentage of nocturnal prescriptions are written for less than six hours, which can potentially disrupt the sleep patterns for the remaining patients in the unit. Medical directors should encourage physicians to write all nocturnal prescriptions for a minimum of six hours. Physicians, registered nurses (RNs) and patient care technicians (PCTs) need to educate patients on the importance of treatment time adherence to achieve the full spectrum of INHD’s clinical and lifestyle benefits. Patients must arrive before a designated lights-out time or, if late, be sent home with treatment deferred until the next day. Finally, physicians should require that any patient who leaves treatment early sign an against medical advice (AMA) form to help limit treatment time non-adherence.

IV. OPTIMAL PATIENT CHARACTERISTICS

Primary characteristics for INHD consideration

- **Concern with fluid removal rate.** INHD can benefit patients who present challenges to safe fluid removal, such as those who require ultrafiltration (UF) at excessive rates (> 10 mL/kg/hr) or those inclined to develop hypotension with volume removal. High UFRs predispose patients to myocardial stunning and ischemic injury from hypoperfusion, which is related to intradialytic hypotension in the setting of uremic reduced capillary density alterations, abnormal vascular autoregulation and preexisting myocardial disease.

- **Intolerance to standard ICHD.** Patients with uncontrolled hypertension or who are on more than three hypertensive medications despite regular hemodialysis may be good INHD candidates. In addition, the modality should be discussed with patients who complain of long post-dialysis recovery times or want to improve libido or general sense of well-being.

- **The desire to maintain employment and avoid work-schedule disruption.** Preserving employment status is a strong consideration for recommending INHD rather than standard ICHD, which may interfere with a patient’s work status. A number of studies have linked continued employment with improved outcomes.

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Additional characteristics

Patients transitioning from chronic kidney disease (CKD) to end stage renal disease (ESRD).
Several characteristics and life-status milestones may make transitioning patients good candidates for INHD, including:

- Living related donors (LRDs) not interested in home modalities
- Employed and not wanting to dialyze at home
- Daytime transportation issues
- High morbidity with hypoalbuminemia, edema, history of congestive heart failure (CHF) and hypotension
- Young age and wanting to preserve health
- Transplant candidates with LVH at baseline, not wanting home dialysis
- Cardiomyopathy ejection fraction < 30% and/or hypotension
- Absence of end-organ damage and a desire to maintain health
- Carpal tunnel and an increase in beta-2-microglobulin

The above characteristics may be supported by the following objective documentation (although these are not required to prescribe INHD):

- Echo: LVH, increased left ventricular mass index (LVMII), increased left ventricular end diastolic volume (LVEDV), increased left atrium (LA), abnormal right ventricle (RV)
- Tilt table, ICHD rounding report: coronary artery disease (CAD) with hypotension, autonomic insufficiency
- Echo, clinical record: edema and CHF with near-term admissions, ejection fraction < 30%
- Lab test: elevated beta-2-microglobulin (> 35 mg/L)
- Clinical history: hypotension (< 90/70 mmHg), malnutrition (albumin < 3.0 g/L), subjective global assessment (SGA) edema, uncontrolled hypertension (> 160/90 mmHg), on multiple medications, not interested in home dialysis
- Transplant lab data: transplantation readiness goals—LRD and CAD (longer waiting time by blood type O)

Prevalent ESRD patients considering a modality transfer. INHD may benefit dialysis patients who want to address co-morbidity risk factors and are unresponsive or fail to improve while on another treatment modality. Potential candidates include:

- Transplant candidates
- On ICHD with
  - CAD and uncontrolled hypertension
  - LVH and uncontrolled hypertension
  - High UF treatment requirements
  - Daytime transportation issues
  - Long recovery and hypotension due to poor ICHD toleration
- Peritoneal dialysis (PD) failure and disinterest in home hemodialysis (HHD)
- Employment demand requiring change in dialysis times
The above characteristics may be supported by the following objective documentation (although these are not required to prescribe INHD):

- ICHD rounding report: UFR > 13 mL/kg/hr, UF intolerance
- Clinical history: long recovery period for ICHD
- Quality metrics data: increased phosphorus (> 6.0 mg/dL) despite medications
- Rounding data and 24-hour ambulatory monitor: uncontrolled hypertension (> 160/90 mmHg) on anti-hypertensive medications, nocturnal non-dipper
- Hospital discharge summary: ICHD patients with three CHF admissions within three months
- PD clinical records: documented PD adequacy and/or UF failure (< 400 mL @ 4 hr with 4.25%)
- Acuity testing: climbing Charlson acuity score (Charlson Comorbidity Index (CCI) > 4)

In selecting patients for INHD, physicians should avoid patients who are too ill and require a level of nursing care that puts too great a burden on a nocturnal staff. Patients who are unable to ambulate into the unit (stretcher patients), who require frequent vital sign checks or are clinically unstable post hospitalization, or warrant other special attention, should not be automatically accepted into INHD programs. In addition, nocturnal programs should generally avoid patients who have behavior problems or are potentially disruptive. Such patients often require excessive attention from dialysis staff and can make the dialysis experience unacceptable to other patients who are trying to sleep. The basic tenet is to avoid patients who pose safety risks on INHD shifts due to level of acuity and care needs.

V. PRESCRIPTION GUIDELINES

While the prescription parameters detailed in literature have minor variations, they are reasonably consistent. In addition, DaVita has outlined an acceptable range for nocturnal dialysis prescriptions, as shown below:

<table>
<thead>
<tr>
<th>Prescription Parameter</th>
<th>Literature Target</th>
<th>Acceptable Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Time (min)</td>
<td>470</td>
<td>360–540</td>
</tr>
<tr>
<td>Dialysate Flow Rate (mL/min)</td>
<td>500</td>
<td>400–600</td>
</tr>
<tr>
<td>Blood Flow Rate (mL/min)</td>
<td>300</td>
<td>200–350</td>
</tr>
<tr>
<td>UFR (mL/kg/hr)</td>
<td>≤ 13</td>
<td>8–13</td>
</tr>
</tbody>
</table>

Additional ancillary items that may be appropriate based on the patient’s individual situation include:

- O2 (2–4 L)
- Chilled dialysate (35–36 °C)
- Dialysate sodium concentration adjustment

Patients with sleeping difficulties, which most often occur during the first few weeks after starting INHD, can benefit from sleep medications—such as temazepam 15 mg or zolpidem 5 mg—as they adjust to the therapy.

Many dialysis patients have sleep apnea and use CPAP devices at home. The devices can generally be used at night in dialysis facilities for patients who need it.
VI. OPERATIONAL CONSIDERATIONS

Adding a nocturnal program to an existing ICHD facility is often an attractive way to improve clinical results, support patients’ lifestyle needs, increase facility capacity and differentiate the DaVita offering from alternative dialysis providers. Facility administrators (FAs), vice presidents (VPs) and regional operations directors (RODs) need to balance the required investment and higher cost structure with the number of patients who would benefit from longer treatment times. They should enlist the support of the medical directors and other physicians who can function as champions to support the therapy. To ensure the success of a nocturnal program, there are several operational considerations.

- **Staffing:** For three-day-a-week INHD programs, shift coverage for nocturnal RNs and PCTs during absences must be addressed. If a nearby nocturnal program is open on alternate days, sharing resources is preferred. However, it is generally necessary to arrange for day-shift clinicians to cover the nocturnal shift.

- **Rounding schedules:** The physician and interdisciplinary team should plan to round at night if possible. This must be discussed early in the planning process to set proper expectations. While DaVita bylaws do not require that physicians round in person in the units at night, and allow patients to be seen each month in the doctors’ office, evening rounding does optimize patient care and it is recommended that physicians visit their INHD patients at least once each month.

- **Patient monitoring:** Special cardiovascular monitoring is typically not required during INHD treatments. While ESRD patients may have an increase in cardiovascular events, additional monitoring—compared to daytime ICHD—is not utilized.

- **Biomed:** Most facilities can support a nocturnal program with no capital investments in their water treatment infrastructure. However, it is necessary to verify water tank capacity, regeneration run cycle and water softener needs with a biomed technician.

- **Cleaning:** For most nocturnal programs (especially six-day programs), the facility cleaning schedule will probably need to be adjusted to before or after the nocturnal shift.

- **Start-up expenses:** Besides marketing expenses, many facilities can support a nocturnal program with minimal additional start-up expenses. However, facilities should evaluate the need for additional investments, such as chair pads, beds, dimmer switches or security cameras on a case-by-case basis.

- **Marketing strategy:** All new nocturnal programs are expected to grow to scale (as a rule of thumb, by approximately 10 patients) within three to six months, because operating at scale reduces the cost premium for therapy administration and optimally leverages existing staff. Achieving that scale can increase the long-term sustainability of the nocturnal program. Local teams should market the nocturnal program to physicians, discharge planners, current regional patients and the local community before starting a program, with follow-ups after the program start date.

VII. SUMMARY

INHD is a unique form of dialysis treatment that is performed in a dialysis center at night for six or more hours. The longer, slower dialysis treatments proffer a variety of clinical and lifestyle benefits, and may be particularly beneficial to certain types of patients, whose characteristics have been outlined in this paper. INHD constitutes a significant opportunity for DaVita both to improve clinical outcomes for patients and to increase capacity at existing dialysis facilities. INHD is a distinctive modality with unique parameters, characteristics and outcomes and, as such, warrants further research and increased medical and operational consideration by the healthcare community.

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