MEDICATION USE EVALUATION OF EDOXABAN IN A TERTIARY HOSPITAL

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Background

- A new oral anticoagulant (NOAC) edoxaban is a reversible direct factor Xa inhibitor.
- Edoxaban, which causes less drug-drug or drug-food interactions than warfarin and does not require routine international normalized ratio (INR) monitoring, is associated with a better safety profile in those with renal impairment or low body weight and the elderly.
- Approved indications for use are :
  1. prophylaxis of stroke and systemic embolism in patients with nonvalvular atrial fibrillation;
  2. treatment of DVT and pulmonary embolism.

Objectives

- To analyze the trend and the appropriateness of edoxaban prescriptions at Samsung Medical Center (SMC) in Korea.
- To search for methods to improve safe and effective use of edoxaban.

Methods

- Retrospective chart review was conducted using the electronic medical records between April 2016 and August 2017.
- Patients who initiated treatment with edoxaban in SMC between April 2016 and August 2016 were included.
- Collected data included age, gender, weight, CrCl, indication, dosage, previous use of other anticoagulants, concomitant medications, adverse drug events, and treatment outcome (defined as confirmed thromboembolism or stroke documentation in chart).
- Data was analyzed to assess if the indications and dosage were appropriate based on the labeling recommendations.

Results

1. Characteristics of subjects (n=142)

- 142 patients were treated with edoxaban during the observation period.

	No.	%
Gender		
Male	87	61.3
Female	55	38.7
Age		
Mean age, years	67	
<65 years	46	32.4
65 ~ 74 years	50	35.2
≥75 years	46	32.4
Weight		
≤60 kg	58	40.8
>60 kg	83	58.5
No data	1	0.7
Previous use of anticoagulants		
Y (Warfarin or NOACs)	94	66.2
N	48	33.8
Creatinine clearance (CrCl, mL/min)		
50 < CrCl	99	69.7
15 ≤ CrCl ≤ 50	40	28.2
CrCl < 15	0	0
No data	3	2.1
CHA_2DS_2-VASc score		
Mean score	3.2	
≤ 1	25	17.6
≥ 2	117	82.4

2. Appropriateness of use (n=142)

Appropriateness of indication	N	%
Appropriate	134	94.4
Prophylaxis of stroke and systemic embolism in patients with nonvalvular atrial fibrillation	133	
Treatment of DVT and pulmonary embolism	1	
Inappropriate*	8	5.6

* 6 patients : for valvular atrial fibrillation
2 patients : for suspected arterial embolism

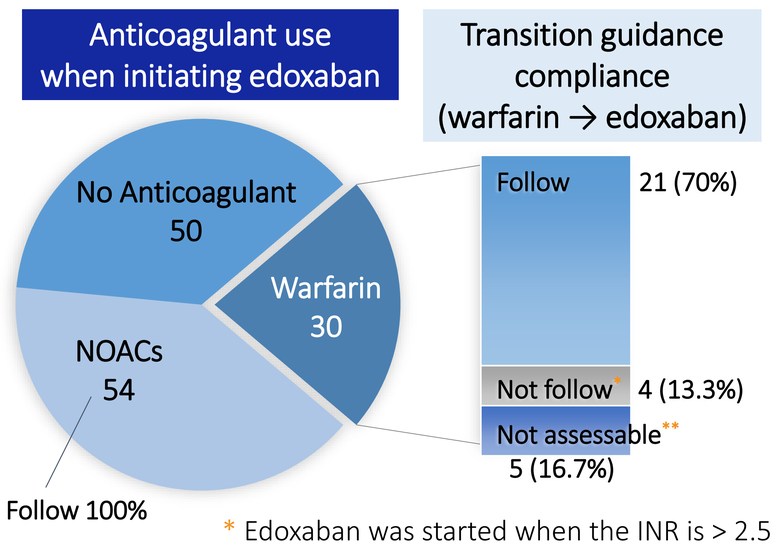
★ *134 patients with appropriate indications were included below.*

3. Analysis of proper indication group (n=134)

1) Before initiating therapy

(1) Assessment of creatinine clearance : 85.8%
(2) Body weight measurement : 94.0%
(3) Transition to edoxaban

<Transition guidance on product labeling>
* Warfarin → Edoxaban : Discontinue warfarin and start edoxaban when the INR is ≤ 2.5.
* Other NOACs → Edoxaban : Discontinue current oral anticoagulant and start edoxaban at the time of the next scheduled dose of the other oral anticoagulant.

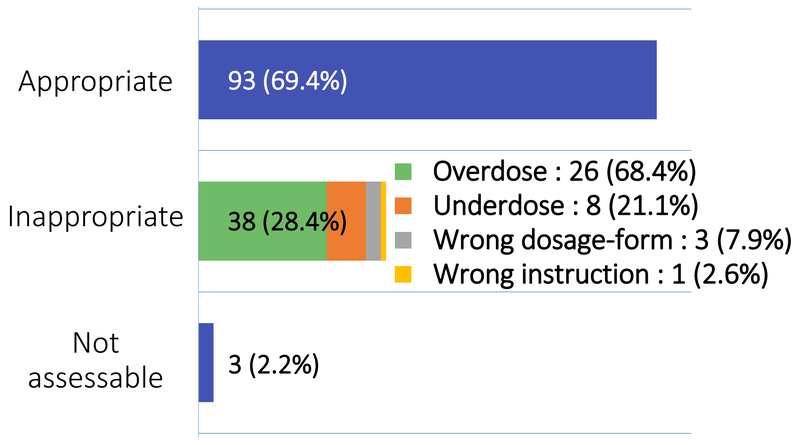


* Edoxaban was started when the INR is > 2.5
** No data of INR

2) Appropriateness of dosing

<Recommended dosing on product labeling>
- The recommended dose : 60 mg once daily.
- 30 mg once daily is recommended in
(1) patients with CrCl 15 to 50 mL/min
(2) patients who weigh less than or equal to 60 kg
(3) patients who are taking certain concomitant P-gp inhibitor medications (cyclosporine, dronedarone, erythromycin, ketoconazole)

(1) Initial dosing



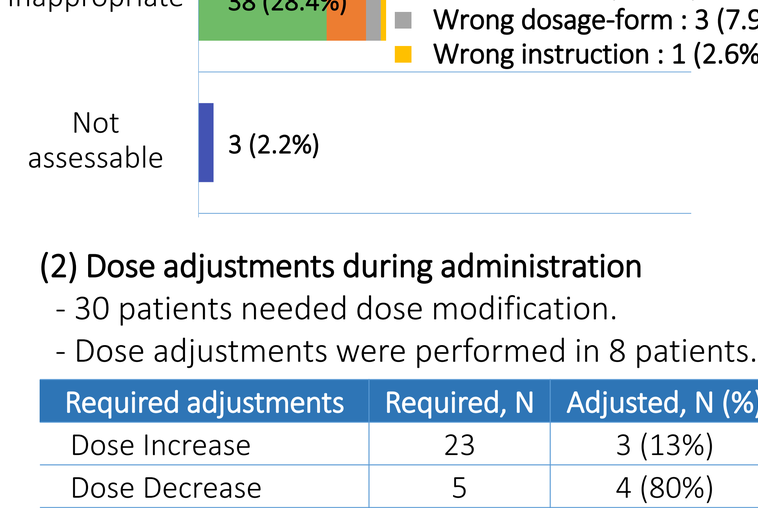
(2) Dose adjustments during administration
- 30 patients needed dose modification.
- Dose adjustments were performed in 8 patients.

Required adjustments	Required, N	Adjusted, N (%)
Dose Increase	23	3 (13%)
Dose Decrease	5	4 (80%)
Formulation change	2	1 (50%)
Total	30	8 (26.7%)

4. Adverse drug events (n=134)

1) Adverse drug events and causes

- Total : 20 patients (14.9%), 30 adverse events
- Bleeding events
  : 14 patients (10.4%), 22 events



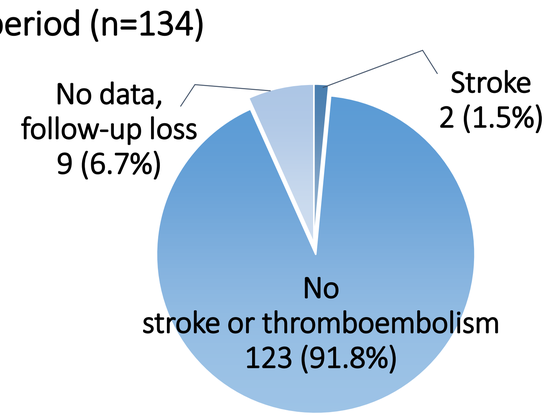
Gastrointestinal	heartburn	2	3
	nausea	1	
Dermatological	rash	1	2
	itching	1	
Miscellaneous	dizziness	2	3
	palpitation	1	

2) Severity and Causality assessment

	Total	Bleeding
Adverse events, N	30	22
CTCAE* grade, N (%)		
Grade 1	21 (70.0)	14 (63.7)
Grade 2	6 (20.0)	5 (22.7)
Grade 3	3 (10.0)	3 (13.6)
WHO probability scale, N (%)		
Probable	9 (30.0)	9 (40.9)
Possible	19 (63.3)	13 (59.1)
Unlikely	2 (6.7)	0

* CTCAE : Common Terminology Criteria for Adverse Events (version 4.03)

5. Treatment outcome during the administration period (n=134)



1) Summary of the stroke cases

	Patient 1	Patient 2
Previous stroke	Y	Y
Previous use of anticoagulants	Warfarin	Rivaroxaban, Apixaban
CHA_2DS_2-VASc	7	4
Body weight (kg)	60	72
CrCl (mL/min)	26	32
Concomitant P-gp inhibitors	N	N
Edoxaban dose (mg)	30	30
Appropriateness of dosing	Y	Y
Interventions after stroke	Maintain (edoxaban)	Switch (to apixaban)

Discussion & Conclusions

- The majority (94.4%) of patients in our study had indications adequate for edoxaban use.
- Of the 30 patients who switched form warfarin to edoxaban, 21 patients initiated edoxaban at the proper time (when the INR is ≤ 2.5).
- 93 of 134 patients (69.4%) received appropriate initial dose based on renal function, body weight, and drug interactions.
- 20 patients (14.9%) had adverse drug events, with a total of 30 events. Of the 30 events, 22 events (73.3%) were bleeding-related events.
- Therefore, pharmacists need to make more efforts to improve the safe and effective use of edoxaban.