Dofetilide Initiation and Monitoring Guideline
University Health System

Initiation of Therapy Restricted to Cardiology Faculty and Fellows

1. Prescription drug coverage/co-pay verification: a. Hospital admission for planned dofetilide initiation: outpatient clinic staff to verify coverage prior to admission b. Unplanned dofetilide initiation (current inpatient status): case management to contact discharge pharmacy (or prescription insurance plan via 1-800-number) to verify coverage	
2. Patient must be admitted or transferred to the 9th floor Sky Tower CICU or ACU.	
3. Patient must be weighed for creatinine clearance calculation.	Weight: _____ kg
4. Diet must contain no grapefruit juice.	
5. Patient must be monitored by continuous ECG monitoring by telemetry.	
6. Patient must have a recent (within 48 hours) serum creatinine measurement. Calculate creatinine clearance. Select dose according to creatinine clearance: • CrCl > 60 mL/min: 500 mcg PO BID • CrCl = 40- 60 mL/min: 250 mcg PO BID • CrCl = 20- <40 mL/min: 125 mcg PO BID • CrCl < 20 mL/min: Dofetilide is contraindicated	Serum Creatinine: _____ mg/dL Creatinine Clearance: _____ mL/min CrCl *(males)*= $\frac{(140\text{-age}) \times \text{body weight in kg}}{72 \times \text{serum creatinine (mg/L)}}$ CrCl *(females)*= $\frac{(140\text{-age}) \times \text{body weight in kg} \times 0.85}{72 \times \text{serum creatinine (mg/dL)}}$
7. Serum potassium must be measured at baseline (within previous 24 hours) and once daily while on dofetilide. If serum potassium < 4 mMol/L, administer supplemental potassium.	Baseline serum potassium: _____ mmol/L Day 2 serum potassium: _____ mmol/L Day 3 serum potassium: _____ mmol/L
8. Serum magnesium must be measured at baseline (within previous 24 hours) and once daily while on dofetilide. If serum magnesium < 2 mg/dL, administer supplemental magnesium.	Baseline serum magnesium: _____ mg/dL Day 2 serum magnesium: _____ mg/dL Day 3 serum magnesium: _____ mg/dL
9. Class I or Class III antiarrhythmic agents should be withheld for at least three (3) half-lives prior to initiating dofetilide. – Bretylium (t½ = 6-13.5 hours*) – Moricizine (t½ = 6.4-13.1 hours) – Disopyramide (t½ = 4-10 hours) – Procainamide (t½ = 2.5-4.7 hours*) – Dronedarone (t½ = 13-19 hours) – Propafenone (t½ = 5-8 hours) – Flecainide (t½ = 7-22 hours) – Quinidine (t½ = 6-7 hours) – Ibutilide (t½ = 2-12 hours) – Sotalol (t½ = 7-18* hours) – Amiodarone (can give if serum amiodarone concentration < 0.3 mg/L or amiodarone has been withdrawn for > 3 months) ** half-life is prolonged in patients with renal dysfunction*	Is the patient currently (or within 3 half-lives) receiving any of these medications? ☐ Yes- Do Not start dofetilide. ☐ No
10. Baseline (within previous 24 hours) 12-lead ECG must be done. If QTc (corrected QT) is > 440 msec (men)/ > 462 (women) (or > 500 msec with ventricular conduction abnormality) DO NOT START DOFETILIDE. (Note: average of 5-10 manual QTc measurements is necessary for accurate QTc assessment in atrial fibrillation)	QT: _____ msec QTc: _____ msec (If heart rate < 60 beats per minute, the QT interval should be used rather than QTc.)
11. A 12-lead ECG must be done 2-3 hours after each of the first five (5) doses. If QTc (corrected QT) after **the first dose** is 15% greater than baseline QTc or is > 500 msec (> 550 msec with ventricular conduction abnormality), adjust dose as follows.	Dose 1 QTc: _____ msec Dose 2 QTc: _____ msec Dose 3 QTc: _____ msec

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– Previous dose = 500 mcg BID then new dose = 250 mcg BID – Previous dose = 250 mcg BID then new dose = 125 mcg BID – Previous dose = 125 mcg BID then new dose = 125 mcg QD If QTc after **doses 2- 5** is > 500 msec (> 550 msec with ventricular conduction abnormality), DISCONTINUE DOFETILIDE. Patients should not be discharged within 12 hours of electrical or pharmacological cardioversion.	Dose 4 QTc: _____ msec Dose 5 QTc: _____ msec (If heart rate < 60 beats per minute, the QT interval should be used rather than QTc.)
12. Check for potential drug interactions. The following medications are ***contraindicated*** for coadministration with dofetilide: – cimetidine – hydrochlorothiazide (with or without triamterene) – ketoconazole – megestrol – prochlorperazine – trimethoprim (or trimethoprim – sulfamethoxazole) – verapamil	Is the patient currently (or within the previous 24 hours) receiving any of these medications? ☐ Yes- Do Not start dofetilide. ☐ No
13. The use of dofetilide with other medications that prolong the QT interval is ***not recommended***. Such medications include: – Phenothiazines *(e.g. chlorpromazine, fluphenazine, perphenazine, prochlorperazine, promethazine, thioridazine)* – Cisapride – Tricyclic antidepressants (*e.g. amitriptyline, desimipramine, doxepin, imipramine, nortriptyline)* – Some oral macrolide antibiotics *(e.g. clarithromycin, erythromycin)* – Some fluoroquinolones	
14. Dofetilide is metabolized to a small extent by the CYP3A4 isoenzyme. Inhibitors of the CYP3A4 could increase systemic dofetilide concentrations. ***Use caution*** if co-administering any of the following drugs with dofetilide:	
– macrolide antibiotics *(clarithromycin, erythromycin)* – azole antifungal agents *(e.g. fluconazole, itraconazole)* protease inhibitors – serotonin reuptake inhibitors – amiodarone – cannabinoids	– diltiazem – grapefruit juice – nefazodone – norfloxacin – quinine – zafirlukast
17. Educational information must be provided and explained to the patient.	Has this been completed? ☐ Yes ☐ No
18. At discharge the patient must be given: – a written prescription – confirmation that their insurance will cover dofetilide	The patient: Has the prescription: ☐ Yes ☐ No Has funding for dofetilide: ☐ Yes ☐ No

Reference:
Dofetilide (Tikosyn®) [package insert]. New York, NY : Pfizer, Inc; 2017.

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