Our Lady of the Lake Regional Medical Center

Cardiology Clinical Pharmacy Service

Dofetilide (Tikosyn®) Pharmacy Consult Protocol on Initiation and Monitoring

Tikosyn® (dofetilide) is a class III antiarrhythmic agent used for the maintenance of normal sinus rhythm in patients with chronic atrial fibrillation or atrial flutter of longer than 1 week duration who have been converted to normal sinus rhythm. Tikosyn® may also be used for conversion of atrial fibrillation and atrial flutter to normal sinus rhythm.

Automatic Consults

Pharmacy will be automatically consulted on all inpatient Dofetilide orders. Clinical pharmacists will automatically monitor and manage dofetilide treatment dosing, as well as potassium and magnesium replacement in all admitted patients using this approved protocol.

Administration

A. Tikosyn® may be ordered in the hospital as a continuation of therapy from home or as a new addition to the patient's medication regimen

    1. New initiation of Tikosyn shall only be ordered by cardiology (including mid-level providers)
    2. Continuation of a home medication may be ordered by any service line provider.

B. Patient receiving **new initiation** therapy must be admitted or transferred into either
    1. Critical care units
    2. Progressive care units
    3. Cardiac Telemetry units

C. Patients receiving **continuation of home** therapy may be admitted to any floor offering continuous telemetry monitoring

D. Prior to verifying a Tikosyn® order (**continuation of home medication or new initiation**), the clinical pharmacist must also review the patient's chart to assess renal function, electrolyte status, drug-drug interactions, QTc interval, and appropriateness of therapy.
    1. If no labs are available, the pharmacist **shall verify and dispense** one dose only and subsequently order a stat BMP and magnesium level.
    2. If serum creatinine, potassium, and magnesium are available **within the previous 30 days**, the pharmacist shall use the reported labs for assessment and verification of the ordered dose but ensure that stat BMP and magnesium level is ordered.
    3. The pharmacist will utilize the Tikosyn order set to order labs, and EKG per protocol

E. Dosing Schedule: Both new starts and home continuation doses will default to 0900 and 2100 for q12h schedule. All doses must be adjusted to ensure every 12 hours interval in situation when the first dose was given outside the default time interval.

Dosage and Monitoring Process

Initiation of TIKOSYN Therapy (New start)

Step 1: EKG assessment: Baseline QTc must be obtained prior to the administration of the first dose. The clinical pharmacist shall utilize an EKG obtained within the 24 hours prior to initiation.

a. If QTc > 440 msec (500msec in patients with ventricular conduction abnormalities) Tikosyn is contraindicated: call and notify physician.

b. If QTc ≤ 440 msec, continue with initiation protocol

Step 2: Creatinine Clearance Calculation: Prior to the first dose administration, calculate creatinine clearance using the Cockcroft-Gault equation for estimating glomerular filtration rate. Actual body weight should be used when calculating creatinine clearance

$$\text{creatinine clearance (male)} = \frac{(140\text{-age}) \times \text{actual body weight in kg}}{72 \times \text{serum creatinine (mg/dL)}}$$

$$\text{creatinine clearance (female)} = \frac{(140\text{-age}) \times \text{actual body weight in kg} \times 0.85}{72 \quad \text{serum creatinine (mg/dL)}}$$

*If serum creatinine is available **within the previous 30 days**, the pharmacist shall use the reported labs for assessment and timely verification of the ordered dose but ensure that stat BMP and magnesium level is ordered*

Step 3: Starting dose based on the calculated creatinine clearance. The Tikosyn® dose should be adjusted for renal function as follows:

Calculated Creatinine Clearance	**Tikosyn® Dose**
> 60 ml/min	500 mcg twice daily
40-60 ml/min	250 mcg twice daily
20- 39 ml/min	125 mcg twice daily
< 20 ml/min	CONTRAINDICATED

Contact Provider for dose adjustment; The provider must approve dose adjustments

The prescribing physician may choose to initiate Tikosyn® at a lower dose than recommended based on the patient's clinical status and baseline QTc.

Step 4: If not ordered, order an EKG 2-3 hours after each dose of dofetilide for the first 6 doses (use Tikosyn order set).

A. If increase in QTc ≤ 15%, continue current dose.

B. If increase in QTc > 15% or > 500 msec (550 msec in patients with ventricular conduction abnormalities) decrease dose (see below):

Dosing adjustments for QTc	
If starting dose is	**Adjusted dose is**
500 mcg BID	250 mcg BID
250 mcg BID	125 mcg BID
125 mcg BID	125 mcg Daily

Contact Provider for dose adjustment; The provider must approve dose adjustments

1 If at any time after the second dose, **QTc increases to greater than 500 msec (550 msec in patients with ventricular conduction abnormalities)**, **Tikosyn® should be discontinued**. Call and notify physician.

2 Patient must be monitored by continuous ECG monitoring by telemetry for a minimum of 72 hours or 12 hours after electrical or pharmacological conversion to normal sinus rhythm, whichever is greater.
3 Any further dose adjustments may be made at the discretion of the ordering physician

Step 5: Clinical pharmacist shall order and monitor potassium and magnesium daily; supplement each electrolyte per approved protocol. (See electrolytes replacement table below)

Continuation of Tikosyn Home medication

Step 1: Patient shall have an EKG obtained upon admission. If the QTc is greater than 500 msec, Tikosyn should be discontinued. Call physician. The clinical pharmacist can utilize an EKG obtained within the previous 7 days prior to admission.

Step 2: Calculate creatinine clearance using the Cockcroft-Gault equation for estimating glomerular filtration rate. Actual body weight should be used when calculating creatinine clearance. Pharmacist must contact provider for adjustments

Step 3: Clinical pharmacist shall order and monitor potassium and magnesium daily; supplement each electrolyte per approved protocol. (See electrolytes replacement table below)

Step 4: Any further dose adjustments may be made at the discretion of the ordering physician

Ordering Labs and EKG

Clinical pharmacist shall use the Tikosyn Oder set to place lab orders for the stat and routine monitoring for the labs and EKG as shown below

- BMP daily
- Magnesium level daily
- EKG, 2 hours after each dose of Tikosyn for the first 6 doses. **Applies to NEW INITIATION THERAPY ONLY**
- Order daily EKG for continuation of Tikosyn home dose

All orders should be entered per protocol under the provider's name

Documentation

A. Clinical pharmacist shall open an I-Vent for all admitted patients on Tikosyn
    - Type: Pharmacy Consult
    - Subtype: Dofetilide
    - Status: Follow-up
B. Ensure daily update of the opened I-vent
C. Clinical pharmacist shall enter an initial progress note and additional notes whenever clinical interventions are implemented, not limited to electrolyte supplementation, dose adjustments, patient education and drug interactions etc.

Tikosyn Patient Education and 7-days supply prior to discharge

A clinical pharmacist shall provide patient education to all patient prior to discharge from the hospital. RXOne pharmacy meds to bed service shall provide a 7-day medication supply to the patient on the day of discharge.

1. Weekday Discharge: On the day of discharge, an electronic prescription for a 7-day supply of Tikosyn® will be send to RXOne pharmacy where the prescription will be filled. The filled prescription along with the Tikosyn®

medication guide and patient education packet shall be hand-delivered to the patient by the RXOne pharmacy team member.

2. Weekend Discharge: For weekend discharge, the nurse will bring a prescription for a 7-day supply of Tikosyn® to the inpatient pharmacy where the prescription will be filled. The filled prescription along with the Tikosyn® medication guide and patient education packet shall be hand-delivered to the clinical pharmacist/pharmacy resident responsible for counseling the patient.

Automatic Potassium and Magnesium Supplementation Guideline

Potassium Level	**Dose to be given**
3.7 to 3.9 mg/dL	Potassium chloride 20 mEq PO x 1 dose
3.0 to 3.6 mg/dL	Potassium chloride 40 mEq PO x 1 dose
less than 3.0 mg/dL	Contact provider

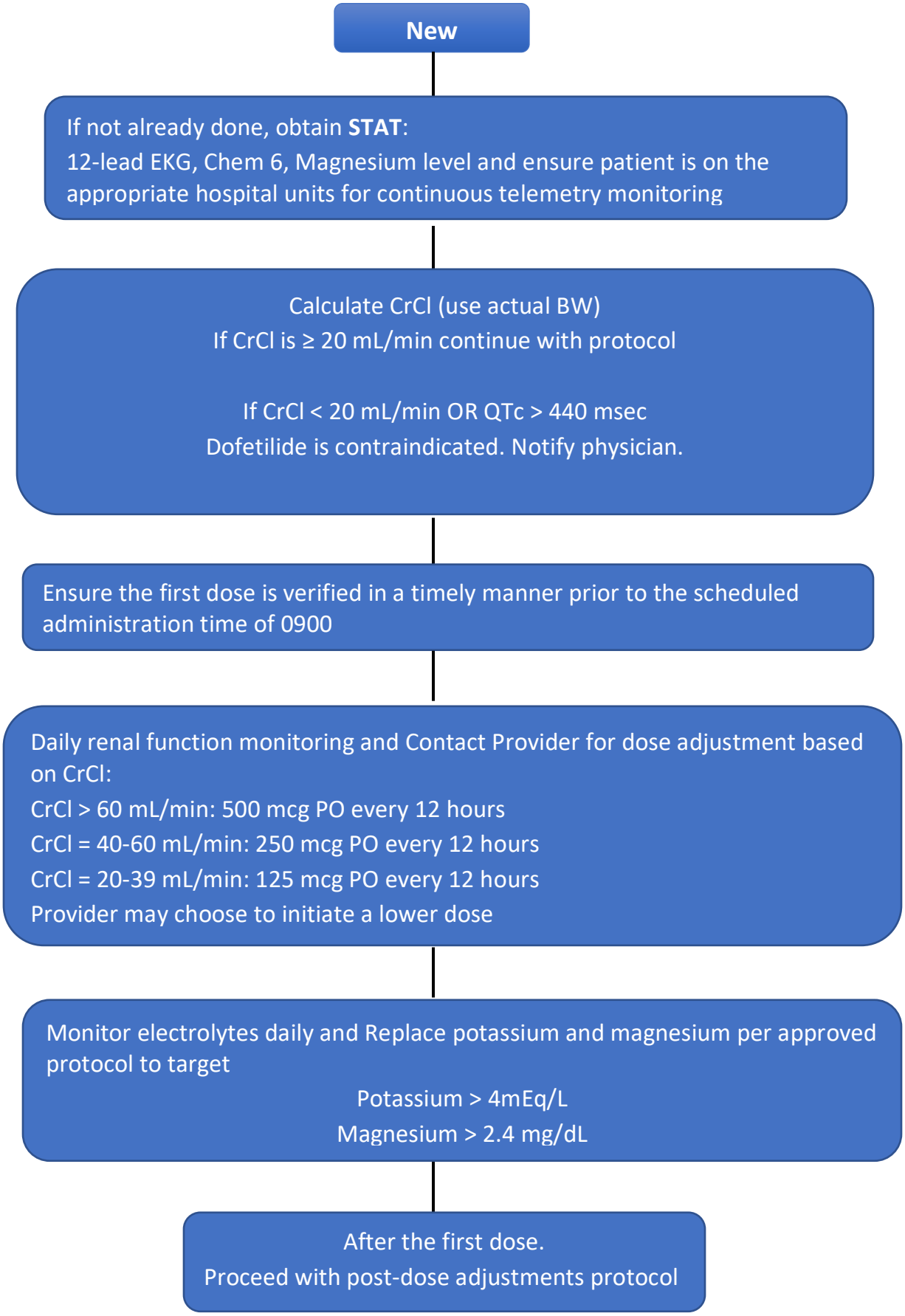
Magnesium Level	**Dose to be given**
1.9 to 2.4 mg/dL	Magnesium oxide 400mg PO x 1 dose
1.5 to 1.8 mg/dL	Magnesium sulfate 2 gm IV x 1 dose
1 to 1.4 mg/dL	Magnesium sulfate 4gm IV x 1 dose
less than 1 mg/dL	Contact provider

Drug interactions with contraindication

Check for potential drug interactions. Tikosyn is contraindicated with co-administration of the following medications

- Verapamil
- Hydrochlorothiazide
- Cimetidine
- Ketoconazole
- Trimethoprim/sulfamethoxazole (or trimethoprim alone)
- Prochlorperazine
- Megestrol
- Dolutegravir
- Biktarvy
- Itraconazole
- Ondansetron

Dofetilide (Tikosyn) Flow chart



Dofetilide post first dose adjustment Flow chart

Ensure EKG is ordered 2 -3 hours after every dose while in the hospital for next 5 doses.

After the 1st dose

A. If increase in QTc ≤ 15%, continue current dose.

B. If increase in QTc > 15% or > 500 msec (550 msec in patients with ventricular conduction abnormalities)

Call physician and recommend decreasing the TIKOSYN dose as follows:

- 500 mcg every 12 hours will be decreased to 250 mcg every 12 hours
- 250 mcg every 12 hours will be decreased to 125 mcg every 12 hours
- 125 mcg every 12 hours will be decreased to 125 mcg daily

After subsequent doses

If at any time after the second dose

QTc increases to > 500 msec (550 msec in patients with ventricular conduction abnormalities)

Tikosyn should be discontinued

Call and notify physician

1. Monitor electrolytes daily and replace potassium and magnesium per approved protocol.
2. Monitor SCr daily to assess changes in renal function. If CrCl changes to a different dosing category, notify physician for dose adjustment
3. Check for drug interactions daily. Notify physician if any noted

This Protocol Review and Revision information

Date of Origination: 02/2022
Last Date Revised: N/A
Last Date Reviewed: 06/2022
P&T committee approval: 06/2022

References

1. Pfizer Laboratories. Tikosyn® Medication Guide. January 2014; Revised 2019
2. Tikosyn® (Dofetilide); Pharmacy Policy, PH-02-22. Our Lady of the Lake Regional Medical Center. Revised September 2021
3. Dofetilide (Lexi-Drugs): Lexicomp®
4. Kibert, J. L., Franck, J. B., Dietrich, N. M., Quffa, L. H., & Franck, A. J. (2019). Impact of a pharmacy-cardiology collaborative management program during initiation of Antiarrhythmic Drugs. *Journal of the American College of Clinical Pharmacy*, *3*(1), 30–35. https://doi.org/10.1002/jac5.1143