Claims

1. A method for preparing crystalline (E)-N-{443-chloro-4-(2-pyridinylmethoxy)anilino]-3-cyano-7-ethoxy-6-quinoliny1)-4-(dimethylamino)-2-butenamide maleate monohydrate comprising the steps of:

i) heating (E)-N- {443-chloro-4-(2-pyridinylmethoxy)anilino]-3-cyano-7-ethoxy-6-quinoliny11-4-(dimethylamino)-2-butenamide free base and maleic acid to 50-60 °C in a water:n-propanol solution, and maintaining the mixture at 50-60 °C for a minimum of 15 min. until a solution is obtained;
ii) cooling said solution over at least one hour to 40 °C and maintaining the cooled solution at 40 °C for 12 hours;
iii) further cooling the cooled solution to room temperature of 25 °C over a minimum of 4 hours and maintaining the further cooled solution at room temperature 25 °C for at least 2 hours; and
iv) filtering the mixture obtained in step iii) to obtain the crystalline (E)-N-{443-chloro-4-(2-pyridinylmethoxy)anilino]-3-cyano-7-ethoxy-6-quinolinyl}-4-(dimethylamino)-2-butenamide maleate monohydrate.

2. The method of claim 1, wherein the obtained crystalline (E)-N-{4-[3-chloro-4-(2-pyridinylmethoxy)anilino]-3-cyano-7-ethoxy-6-quinoliny1}-4-(dimethylamino)-2-butenamide maleate monohydrate is characterized by X-ray diffractionpeaks at the following angles ±0.20° of 20 in its X-ray diffraction pattern: 6.53, 8.43, 10.16, 12.19, 12.47, 13.01,15.17, 16.76, 17.95, 19.86, 21.11, 21.88, 23.22, 23.78, 25.69, 26.17, 27.06, 27.58, 28.26, 28.73, and 29.77.

3. The method of claim 2, wherein the obtained crystalline (E)-N-{4-[3-chloro-4-(2-pyridinylmethoxy)anilino]-3-cyano-7-ethoxy-6-quinoliny1}-4-(dimethylamino)-2-butenamide maleate monohydrate has substantially the X-ray diffraction pattern as shown in Fig. 7.

4. The method of claim 2 or 3, wherein the X-ray diffraction pattern has been collected with a voltage of 40 kV and a current of 40.0 mA, at 5.00-30.00 degree scan range in a Bruker 08 Advance instrument with a scan step size of 0.01° and total scan time of 30 minutes, using a Vantec-1 detector and a Ni filter.

5. Method according to any one of claims 2 to 4, wherein the crystalline neratinib maleate monohydrate is further **characterized by** a DSC-plot with two thermal events at 109.63°C and 203.81°C peak temperature.

6. The method according to any one of claims 1 to 5, wherein the obtained crystalline (E)-N-{4-[3-chloro-4-(2-pyridinylmethoxy)anilino]-3-cyano-7-ethoxy-6-quinoliny1}-4-(dimethylamino)-2-butenamide maleate monohydrate exhibits water loss at about 50°C, as measured by DSC, and is characterized by a water content of 2.5 to 2.7% by weight, as measured by thermal gravimetric analysis, based on the weight of the compound as a monohydrate.