DOPHARMA

Solubility of Doxylin® 100% in drinking water

WpH corrector (citric acid) is often used to condition the water in order to improve the solubility and stability of doxycycline in a solution. This is achieved by lowering the pH of the solution and scavenging two- and trivalent ions.

1. Lowering the pH of the solution

The solubility of doxycycline is optimal at a low pH (<3). A concentrated pre-solution with 100 – 200 grams of doxycycline dissolved in ten litres of water will have a sufficiently low pH. The pH will however rise if this pre-solution is diluted. In that case solubility may become a problem. Lowering the pH with WpH corrector will improve solubility in the medicated drinking water.

2. Scavenging two-and trivalent ions

Doxycycline dissolved without water conditioner will often precipitate within one or two hours. This is caused by the formation of complexes of doxycycline with calcium (Ca), magnesium (Mg) and iron (Fe). WpH corrector scavenges these ions so they can no longer form complexes with doxycycline. This explains why WpH corrector is preferred over other acids like hydrochloric acid which does not have the capacity to scavenge these ions.

To use doxycycline and the WpH corrector correctly there are three parameters which have to be evaluated to determine the right amount of WpH corrector.

1. Amount of doxycycline

WpH corrector is often satisfactorily used in a ratio of 1 : 1 with doxycycline. In this case, if 100 gram of Doxylin® 100% is dissolved in 10 litres of drinking water, 100 gram of WpH corrector should first be added to the drinking water.

2. Amount of water

Doxycycline is a powder with a low pKa. When dissolved in water, the pH of the solution will decrease. However, when a large volume of water is used for the pre-solution, this will result in a more diluted solution with a higher pH. More WpH corrector will then be needed to lower the pH to the desired level.

3. Quality of the drinking water

Particularly the pH and hardness of the water are important when considering the amount of WpH corrector needed. In general, the higher the pH and the water hardness, the more WpH corrector is required to obtain a solution with a good stability. The ratio of doxycycline to WpH corrector in relation to the water hardness is given in Table 1.

Table 1 Ratio of WpH corrector to doxycycline dependent on the water hardness.

Water hardness		Doxycycline : WpH corrector
Normal	7 – 14 °D	1 : 1
Hard	14 – 21 °D	1 : 1 ½
Very hard	> 21 °D	1 : 2

Finally, the amount of citric acid already incorporated in the product has to be taken into account. Doxylin® 50% WSP already contains citric acid (18.3 %) and adding extra WpH corrector is usually not necessary. However, when solubility problems are to be expected, an additional 317 gram WpH corrector can be added per kg of the product to obtain a ratio of 1 : 1.

The use of WpH corrector will not only increase the stability of doxycycline in a solution, but it might also enhance the absorption of doxycycline from the gastrointestinal tract. This can possibly result in higher plasma concentrations and can therefore influence the rate of elimination of doxycycline.

