

OXANDROLONE (OXANDRIN) USE AND THE INTERACTION WITH WARFARIN

Robert H. Demling, M.D.

Brigham and Women's Hospital

Professor of Surgery

Harvard Medical School

Boston, MA

I. INTRODUCTION

Oxandrin®, manufactured by Savient Pharmaceuticals, Inc., is an FDA approved anabolic steroid (oxandrolone) used to treat involuntary weight loss caused by acute or chronic injury, illness or infection. This anabolic steroid has the benefit of being metabolized by the kidney rather than in the liver, like the other anabolic steroids, making it safer for use in sick patients. Over the past five years Oxandrin® has proven to be of considerable benefit for treating the common complication of involuntary weight loss, especially loss of body muscle, in a variety of patient populations including major burns, acute and chronic wounds, the elderly with weight loss, HIV positive patients and cancer patients on chemotherapy. Several recent randomized prospective trials have documented significant improvements in restoration and maintenance of body weight, mainly lean body mass or muscle, along with decreased hospital stay and improved wound healing using Oxandrin® to treat involuntary weight loss compared with standard nutritional therapy alone.

However, there is a well recognized potentially hazardous side effect, which must be recognized. Oxandrolone produces an increased sensitivity to warfarin. The risk of this drug interaction, causing a bleeding state in patients, has been substantially diminished by the research of Savient. A clinical study has shown that the warfarin dose should be decreased by 80% when using Oxandrin® 10mg pills. This guideline has now been implemented in clinical practice. This safety information is of significant benefit in my practice, managing severe burns and wounds as excessive bleeding in the subpopulation of patients on both drugs would be a major complication.

II. EXPERIENCE WITH THE USE OF OXANDRIN

Involuntary Weight Loss (IWL), especially loss of lean body mass or muscle, is a common complication of acute and chronic injury, illness or infection. The degree of weight loss corresponds with the magnitude of the resulting complications ranging from increased infection risk and impaired wound healing to death from "wasting." This problem is particularly prevalent in the major burn and wound population where rapid muscle breakdown is a well recognized metabolic response to the injury even with good nutrition. The ability to treat and control this deleterious response, with the use of an anabolic steroid oxandrolone, has resulted in substantial patient care benefits, and indeed has saved lives.

I have been using Oxandrin® in this burn-wound population for the past 6 years. In addition, I have extensively studied and published the benefits of oxandrolone use with seven randomized prospective trials. Other clinical investigators have also documented the improved restoration of IWL and improved outcome when using oxandrolone. A multicenter prospective randomized double-blind trial has recently demonstrated that Oxandrin® significantly decreased the length of hospital stay in severely burned patients.

I have also reported on the benefits and safety of Oxandrin® in the geriatric burn patient population, whose average age is 75 years. In this population warfarin use is more common and the appropriate safety measures – significant decrease in warfarin dosing, per Savient's instructions – have been carried out, resulting in no bleeding complications.

I have also successfully used Oxandrin® extensively in the chronic wound population with pre-existing involuntary weight loss, the majority of patients being elderly, and

with pre-existing disorders such as cardiovascular disease and diabetes. This population includes patients on warfarin for a vascular thrombosis disorder (deep vein thrombosis) and post cardiac surgery.

III. SUBPOPULATION OF WARFARIN AND OXANDROLONE

The major indications for warfarin use would first be heart problems such as atrial fibrillation, post-heart attack with evidence of embolization, and post-replacement of a heart valve. These problems and procedures are more likely present in the elderly population. The second and common indication would be for the treatment of deep vein thrombosis (DVT) especially with evidence of pulmonary emboli. Deep vein thrombosis is more commonly seen after a surgical procedure in the elderly or in a chronically ill patient caused by lack of mobility. DVT also occurs in the cancer patient population and burn patient population, as their blood is more prone to excessive clotting. Major complications of warfarin use are hemorrhage and anticoagulation; these must be very tightly regulated, as warfarin has a very narrow therapeutic range.

The incidence of IWL is very high in this same population, i.e. the elderly, especially with wounds, chronic disability, and cancer patients, resulting in a significant sub-population of patients who would be on both drugs. The number of burns in the geriatric and disabled population is definitely increasing, first because the increased risk of a home accident or burn and secondly because the size of this population is growing (the aging of America).

Another group of patients making up this sub-population would be post-surgical cancer patients on chemotherapy with IWL and a diagnosis of thrombosis. The

incidence of deep vein thrombosis is also significant in the acute trauma and burn population where oxandrolone is used.

Because bleeding is a severe complication, the specific guidance from Savient regarding the Oxandrin® and warfarin interaction and dosing must be followed. The recommended 80% decrease in warfarin dosing indicates a very large drug interaction. I am not aware of any other drug interaction besides the oxandrolone - warfarin interaction with or even approaching such a large change required in dosing.

I have reviewed the Savient research document which explains this effect and which is the basis of the recommendations. The clinical study is very well done and the recommendations are very valuable as I have explained in this statement.

IV. THE PROBLEM OF GENERIC OXANDROLONE AND WARFARIN

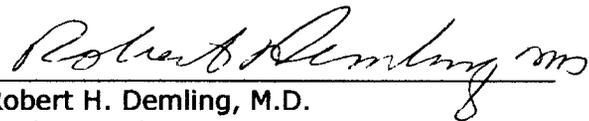
The use of a generic oxandrolone would be of significant concern if it's interaction with warfarin is not precisely studied, as has been done with Savient's Oxandrin®. The generic drug would most certainly not have the exact same potency and pharmacological activity as Oxandrin®. Therefore, the Savient guidelines for warfarin and oxandrolone use should not be applied to a generic drug, and should not be relied upon by a physician in this prescribing. The generic manufacturer would need to develop it's own guidelines.

Of concern is the fact that hospital, chronic care and private pharmacies could substitute a generic without notification of the treating physician. Therefore, if the interaction of warfarin with a generic are different, this situation would be potentially

dangerous, as the treating physician may not know which brand of oxandrolone was being dispensed.

V. SUMMARY

Oxandrolone (Oxandrin®) is a very valuable and safe drug to use for managing involuntary weight loss in a variety of patient populations. Currently the main concern with usage of oxandrolone along with warfarin, i.e. bleeding, has been addressed in clinical studies by Savient and the current recommendations can prevent this complication. This statement could not be made with the use of a generic unless a set of specific guidelines were also developed for the use of each generic oxandrolone for use with warfarin and also that a system be in place to make sure the treating physician knew which oxandrolone products were being used and what the appropriate guidelines were for that product.



Robert H. Demling, M.D.
Professor of Surgery
Brigham and Women's Hospital
Harvard Medical School