

# The Use of Topical 5-Fluorouracil in Children

Commercially-available topical fluorouracil is indicated for use in adults. When the products were brought to market, the studies only established its safety and efficacy in patients over the age of 18. However, this agent has documented use in children under the age of 18. The purpose of this document is to highlight the uses of topical 5-fluorouracil in children, adverse effects reported in young patients, and pharmacokinetic parameters.



There are reports in the literature that topical 5-fluorouracil has been used for various indications in patients under the age of 18. Pediatric patients were included a group treated for squamous cell carcinoma secondary to xeroderma pigmentosum. The average treatment duration was for six months.<sup>1</sup> Children aged 2-19 were treated for chromoblastomycosis (a granulomatous disease of the skin caused by dematiaceous fungi) with topical 1% fluorouracil. They were treated for up to three months.<sup>2</sup> In a 13 year old girl with a 4-year history of erythematous nodules and plaques on her trunk and limbs. Five percent 5-fluorouracil topical cream along with coal tar applied for six months resulted in the clearance of the lesions.<sup>3</sup>

Pediatric patients were also included in a study using variable strengths of fluorouracil (0.5%-5.0) along with salicylic acid to treat plantar warts. Treatment lasted an average of two months, although one patient was treated up to seven months.<sup>4</sup> A trial for viral warts using 5% 5-fluorouracil ointment included children (age 5 to 14) and showed statistically significant results versus placebo with the 5-fluorouracil (60% vs. 16.7%;  $p < 0.001$ ). There was also a greater efficacy with children compared to adults.<sup>11</sup>

Long term use has also been documented in children. A case report of a child with basal cell nevus syndrome shows successful management of the disease with a combination of topical fluorouracil and tretinoin applied over the duration of ten years.<sup>5</sup>

*Continued on back page...*



May 2007  
Updated Jan 2008



The adverse effects associated with topical fluorouracil use in the above studies were skin dryness<sup>1</sup>, a slight burning sensation<sup>3</sup>, pruritis<sup>3</sup>, and local dermatitis.<sup>4</sup> The listed adverse effects in adults were: burning, crusting, allergic contact dermatitis, erosion, erythema, hyperpigmentation, irritation, pain, photosensitivity, pruritis, scarring, rash, soreness and ulceration.<sup>6</sup> A major side effect of onycholysis was shown to occur equally between children and adults.<sup>11</sup>

No studies have been done to assess the pharmacokinetics of topical fluorouracil when used in patients under the age of eighteen. At the age of one year, skin permeability is similar to that of an adult.<sup>7</sup> The absorption of 5-fluorouracil would be greatly increased in patients younger than one year old. The dermis of newborns has less keratin and therefore less of a protective barrier.<sup>8</sup> Topical medications should be avoided if possible in patients less than 6 months old.<sup>9</sup>

There is also a low risk of systemic toxicity with topical fluorouracil. According to the manufacturer of Efudex, approximately 5.98% of the topical 5% preparation is absorbed systemically. Patients exhibited no toxicity signs during this study<sup>10</sup>. A study done in rats determined that the LD50 of topical fluorouracil to 500mg/kg<sup>10</sup>. The standard dispensing quantity for WartPeel is 5 grams which will contain a total of 100mg of 5-fluorouracil.

Although use of topical fluorouracil in children is not currently approved by the FDA, it may be reasonable due to the low systemic absorption expected.



#### References:

1. Hamouda B, Jamila Z, Najet R, et al. "Topical 5-fluorouracil to treat multiple of unresectable facial squamous cell carcinomas in xeroderma pigmentosum." *J Am Acad Dermatol.* 2001;44(6):1054.
2. Perez-Blanco M, Hernandez Valles R, Garcia-Humbria L, Yegres F. "Med Mycol." 2006 Aug;44:467-71.
3. Rodriguez-Jurado R, Vidaurri-de la Cruz H, Duran-Mckinster C, Ruiz-Maldonado R. "Indeterminate Cell Histiocytosis." *Arch Pathol Lab Med.* 2003;127(6):748-51.
4. Young S, Cohen G. "Treatment of Verruca Plantaris with a Combination of Topical Fluorouracil and Salicylic Acid." *J Am Podiatr Med Assoc.* 2005;95(4):366-9.
5. Strange PR, Lang PG. "Long-term management of basal cell nevus syndrome with topical tretinoin and 5-fluorouracil." *J Am Acad Dermatol.* 1992 Nov;27(5 Pt 2):842-5.
6. "Efudex." *Mosby's Drug Consult.* Accessed online through Stat!Ref on 4/20/07.
7. "Children's Environmentation Health Project: Dermatological Effects." Accessed online at [www.cape.ca/children/derm1.html](http://www.cape.ca/children/derm1.html) on 4/20/07.
8. Bearer CF. "How are children different from adults?" *Environ Health Perspec.* 1995;103:7-12.
9. "Integumentary Alterations". *Pediatric Nursing: Caring for Children and their Families.* Accessed online through Stat!Ref on 4/20/07.
10. Gladsjo JA, Alió Sáenz AB, Bergman J, Kricorian G, Cunningham BB. University of California, San Diego, California, USA. *Pediatr Dermatol.* 2009 May-Jun; 26(3):279-85.
11. Hursthouse MW. "A controlled trial on the use of topical 5-fluorouracil on viral warts." *British Journal of Dermatology.* 1975;92:93-6.

309 Court Ave. Ste. 250 • Des Moines, IA 50309 • ph. 855.409.5496

**www.wartPEEL.com**