SECTION-1: Identification of the substance / mixture and the company / undertaking

Catalogue Number	CS-O-11195
Product Name	Efinaconazole
CAS No.	164650-44-6
Category	API
Synonyms	-
Brand	Clearsynth Labs Ltd.
Identified uses	Laboratory Chemicals
Uses advised against	Not available
Company	Clearsynth Labs Ltd. Mumbai, India
Emergency Phone #	+91-22-245045900
REACH No.	Not available

SECTION 2: Hazards identification

Disclaimer: This is sample MSDS. Please email **sales@clearsynth.com** for more details.

2.1 Classification of the substance or mixture-Regulation (EC) No 1272/2008:

Not available

2.2 Label Elements

Signal Word: Warning

Not available

Hazard Statement(s)

Code	Statement
H361	Not available

Precautionary Statement(s)

Code	Statement
P203	Not available
P280	Wear protective gloves/protective clothing/eye protection/face protection.
P318	Not available

P405	Store locked up.
P501	Dispose of contents/container in accordance with local/regional/national/international regulatio

SECTION 3: Composition / information on ingredients

3.1 Substance

Component : Efinaconazole
CAS Number : 164650-44-6
Molecular Formula : C18H22F2N4O
Molecular Weight : 348.4
Parent Chemical : Efinaconazole
Synonyms : -
Concentration : Not available

SECTION 4: First aid measures

Not available

SECTION 5: Firefighting measures

Not available

SECTION 6: Accidental release measures

Not available

SECTION-7: Handling and storage

Not available

SECTION 8: Exposure controls / personal protection

Not available

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Test	Result
Appearance	White solid
IR spectrum	No data available

Test	Result
pH	No data available
Solubility	In DMSO

Property	Value
a) Physical State	No data available
b) Color	No data available
c) Odor	No data available
d) pH	No data available
e) Vapour Pressure	No data available
f) Viscosity	No data available
g) Initial Boiling Point and boiling range	No data available
h) Melting Point / Freezing Point	No data available
i) Auto Ignition Temperature	No data available
j) Flash Point	No data available
k) Explosion Limit, Lower	No data available
l) Explosion Limit, Upper	No data available
m) Decomposition Temperature	No data available
n) Loss on Drying	No data available
o) Relative Density	No data available
p) Solubility (in DMSO)	No data available
q) Oxidizing Properties	No data available

SECTION 10: Stability and reactivity

Not available

SECTION 11: Toxicological information

11.1 Information on toxicological effects
- Acute toxicity: IDENTIFICATION AND USE: Efinaconazole is used as antifungal agent. It is indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. HUMAN EXPOSURE AND TOXICITY: Efinaconazole 10% solution did not cause contact sensitization and induced

only minimal skin irritation in human studies. ANIMAL STUDIES: Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. In 13 week dermal toxicity in mice, an increase in liver weight and minimal to mild panlobular hepatocellular hypertrophy was observed, the local application of the drug and/or the vehicle alone resulted in higher incidences of hyperkeratosis, epidermal hyperplasia, and mononuclear infiltrates in the treated skin. Higher concentration of the test article were associated with higher severity of these cutaneous changes compared to controls, and a low incidence of the formation of erosion/ulcers at the treated site. Efinaconazole 10% solution applied intratympanically to the guinea pig middle ear caused significant middle ear inflammation and hearing impairment. In dermal toxicity studies, efinaconazole was well tolerated in minipigs at doses up to 150-200 mg /kg/day. Slight to moderate skin reactions were noted macroscopically and microscopically in all test article groups and vehicle control and consisted of hyperkeratosis, acanthosis and localized inflammation. These skin effects were attributed to the vehicle and were not considered adverse due to the mild severity of changes. A 2-year dermal carcinogenicity study in mice was conducted with daily topical administration of 3%, 10% and 30% efinaconazole solution. Severe irritation was noted at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinaconazole. The high dose group was terminated at week 34 due to severe skin reactions. No drug-related neoplasms were noted at doses up to 10% efinaconazole solution (248 times the MRHD based on AUC comparisons). In a pre- and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day efinaconazole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryofetal toxicity (increased pre-natal pup mortality, reduced live litter sizes and increased post-natal pup mortality) was noted at 25 mg/kg/day. No embryofetal toxicity was noted at 5 mg/kg/day (17 times the MRHD based on AUC comparisons). No effects on post-natal development were noted at 25 mg/kg/day (89 times the MRHD based on AUC comparisons). Subcutaneous doses of 1, 5, and 10 mg/kg/day efinaconazole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rabbits. In the presence of maternal toxicity, there was no embryofetal toxicity or malformations at 10 mg/kg/day (154 times the MRHD based on AUC comparisons). Efinaconazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay). /LABORATORY ANIMALS: Acute Exposure/ Assessments of efinaconazole acute toxicity were conducted in rat via dermal and subcutaneous (SC) administration, in mice via intraperitoneal administration, and in dog via dermal administration. Efinaconazole was well tolerated in both genders of all 3 species, with all LD50 values higher than 0.5 to 2 grams/kg.

- Skin corrosion/irritation: IDENTIFICATION AND USE: Efinaconazole is used as antifungal agent. It is indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. HUMAN EXPOSURE AND TOXICITY: Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in human studies. ANIMAL STUDIES: Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. In 13 week dermal toxicity in mice, an increase in liver weight and minimal to mild panlobular hepatocellular hypertrophy was observed, the local application of the drug and/or the vehicle alone resulted in higher incidences of hyperkeratosis, epidermal hyperplasia, and mononuclear infiltrates in the treated skin. Higher concentration of the test article were associated with higher severity of these cutaneous changes compared to controls, and a low incidence of the formation of erosion/ulcers at the treated site. Efinaconazole 10% solution applied intratympanically to the guinea pig middle ear caused significant middle ear inflammation and hearing impairment. In dermal toxicity studies, efinaconazole was well tolerated in minipigs at doses up to 150-200 mg /kg/day. Slight to moderate skin reactions were noted macroscopically and microscopically in all test article groups and vehicle control and consisted of hyperkeratosis, acanthosis and localized inflammation. These skin effects were attributed to the vehicle and were not considered adverse due to the mild severity of changes. A 2-year dermal carcinogenicity study in mice was

conducted with daily topical administration of 3%, 10% and 30% efinaconazole solution. Severe irritation was noted at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinaconazole. The high dose group was terminated at week 34 due to severe skin reactions. No drug-related neoplasms were noted at doses up to 10% efinaconazole solution (248 times the MRHD based on AUC comparisons). In a pre- and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day efinaconazole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryofetal toxicity (increased pre-natal pup mortality, reduced live litter sizes and increased post-natal pup mortality) was noted at 25 mg/kg/day. No embryofetal toxicity was noted at 5 mg/kg/day (17 times the MRHD based on AUC comparisons). No effects on post-natal development were noted at 25 mg/kg/day (89 times the MRHD based on AUC comparisons). Subcutaneous doses of 1, 5, and 10 mg/kg/day efinaconazole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rabbits. In the presence of maternal toxicity, there was no embryofetal toxicity or malformations at 10 mg/kg/day (154 times the MRHD based on AUC comparisons). Efinaconazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay). /HUMAN EXPOSURE STUDIES/ Onychomycosis is a chronic condition that often requires long-term management to eradicate the causative fungus, allow a healthy nail to grow, and prevent relapse. As a successful outcome depends highly on patient adherence with treatment, a low risk of periungual skin irritation with topical medication is clinically relevant. /The purpose of this research was/ to study the potential for efinaconazole 10% solution and its corresponding vehicle to induce delayed contact skin sensitization and evaluate its skin irritation potential. Efinaconazole 10% solution and its vehicle were studied in 239 healthy volunteers for the potential to induce contact skin sensitization. This included a series of induction, challenge, and re-challenge phases. An additional 21-day cumulative irritation study was undertaken in 35 healthy volunteers to compare three concentrations of efinaconazole (1%, 5%, and 10%), vehicle, and positive/negative controls. There was no evidence of induced contact sensitization under occlusive, semi-occlusive, and open (open rub-in) applications of efinaconazole 10% solution. Efinaconazole 1%, 5%, and 10% solutions have mean cumulative irritancy indices of 1.12, 1.26, and 1.18, respectively, where a range of >0 to =1 is classified as "mildly irritating." Results were comparable to vehicle (1.04). Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in the studies completed.

- Serious eye damage/eye irritation: No data available.
- Respiratory or skin sensitization: IDENTIFICATION AND USE: Efinaconazole is used as antifungal agent. It is indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. HUMAN EXPOSURE AND TOXICITY: Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in human studies. ANIMAL STUDIES: Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. In 13 week dermal toxicity in mice, an increase in liver weight and minimal to mild panlobular hepatocellular hypertrophy was observed, the local application of the drug and/or the vehicle alone resulted in higher incidences of hyperkeratosis, epidermal hyperplasia, and mononuclear infiltrates in the treated skin. Higher concentration of the test article were associated with higher severity of these cutaneous changes compared to controls, and a low incidence of the formation of erosion/ulcers at the treated site. Efinaconazole 10% solution applied intratympanically to the guinea pig middle ear caused significant middle ear inflammation and hearing impairment. In dermal toxicity studies, efinaconazole was well tolerated in minipigs at doses up to 150-200 mg /kg/day. Slight to moderate skin reactions were noted macroscopically and microscopically in all test article groups and vehicle control and consisted of hyperkeratosis, acanthosis and localized inflammation. These skin effects were attributed to the vehicle and were not considered adverse due to the mild severity of changes. A 2-year dermal carcinogenicity study in mice was conducted with daily topical administration of 3%, 10% and 30% efinaconazole solution. Severe irritation was noted

at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinaconazole. The high dose group was terminated at week 34 due to severe skin reactions. No drug-related neoplasms were noted at doses up to 10% efinaconazole solution (248 times the MRHD based on AUC comparisons). In a pre- and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day efinaconazole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryofetal toxicity (increased pre-natal pup mortality, reduced live litter sizes and increased post-natal pup mortality) was noted at 25 mg/kg/day. No embryofetal toxicity was noted at 5 mg/kg/day (17 times the MRHD based on AUC comparisons). No effects on post-natal development were noted at 25 mg/kg/day (89 times the MRHD based on AUC comparisons). Subcutaneous doses of 1, 5, and 10 mg/kg/day efinaconazole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rabbits. In the presence of maternal toxicity, there was no embryofetal toxicity or malformations at 10 mg/kg/day (154 times the MRHD based on AUC comparisons). Efinaconazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay). /HUMAN EXPOSURE STUDIES/ Onychomycosis is a chronic condition that often requires long-term management to eradicate the causative fungus, allow a healthy nail to grow, and prevent relapse. As a successful outcome depends highly on patient adherence with treatment, a low risk of periungual skin irritation with topical medication is clinically relevant. /The purpose of this research was/ to study the potential for efinaconazole 10% solution and its corresponding vehicle to induce delayed contact skin sensitization and evaluate its skin irritation potential. Efinaconazole 10% solution and its vehicle were studied in 239 healthy volunteers for the potential to induce contact skin sensitization. This included a series of induction, challenge, and re-challenge phases. An additional 21-day cumulative irritation study was undertaken in 35 healthy volunteers to compare three concentrations of efinaconazole (1%, 5%, and 10%), vehicle, and positive/negative controls. There was no evidence of induced contact sensitization under occlusive, semi-occlusive, and open (open rub-in) applications of efinaconazole 10% solution. Efinaconazole 1%, 5%, and 10% solutions have mean cumulative irritancy indices of 1.12, 1.26, and 1.18, respectively, where a range of >0 to =1 is classified as "mildly irritating." Results were comparable to vehicle (1.04). Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in the studies completed.
- Germ cell mutagenicity: IDENTIFICATION AND USE: Efinaconazole is used as antifungal agent. It is indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. HUMAN EXPOSURE AND TOXICITY: Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in human studies. ANIMAL STUDIES: Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. In 13 week dermal toxicity in mice, an increase in liver weight and minimal to mild panlobular hepatocellular hypertrophy was observed, the local application of the drug and/or the vehicle alone resulted in higher incidences of hyperkeratosis, epidermal hyperplasia, and mononuclear infiltrates in the treated skin. Higher concentration of the test article were associated with higher severity of these cutaneous changes compared to controls, and a low incidence of the formation of erosion/ulcers at the treated site. Efinaconazole 10% solution applied intratympanically to the guinea pig middle ear caused significant middle ear inflammation and hearing impairment. In dermal toxicity studies, efinaconazole was well tolerated in minipigs at doses up to 150-200 mg /kg/day. Slight to moderate skin reactions were noted macroscopically and microscopically in all test article groups and vehicle control and consisted of hyperkeratosis, acanthosis and localized inflammation. These skin effects were attributed to the vehicle and were not considered adverse due to the mild severity of changes. A 2-year dermal carcinogenicity study in mice was conducted with daily topical administration of 3%, 10% and 30% efinaconazole solution. Severe irritation was noted at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinaconazole. The high dose group was terminated at week 34 due to severe skin reactions. No

drug-related neoplasms were noted at doses up to 10% efinaconazole solution (248 times the MRHD based on AUC comparisons). In a pre- and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day efinaconazole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryofetal toxicity (increased pre-natal pup mortality, reduced live litter sizes and increased post-natal pup mortality) was noted at 25 mg/kg/day. No embryofetal toxicity was noted at 5 mg/kg/day (17 times the MRHD based on AUC comparisons). No effects on post-natal development were noted at 25 mg/kg/day (89 times the MRHD based on AUC comparisons). Subcutaneous doses of 1, 5, and 10 mg/kg/day efinaconazole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rabbits. In the presence of maternal toxicity, there was no embryofetal toxicity or malformations at 10 mg/kg/day (154 times the MRHD based on AUC comparisons). Efinaconazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay).
- Carcinogenicity: IDENTIFICATION AND USE: Efinaconazole is used as antifungal agent. It is indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. HUMAN EXPOSURE AND TOXICITY: Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in human studies. ANIMAL STUDIES: Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. In 13 week dermal toxicity in mice, an increase in liver weight and minimal to mild panlobular hepatocellular hypertrophy was observed, the local application of the drug and/or the vehicle alone resulted in higher incidences of hyperkeratosis, epidermal hyperplasia, and mononuclear infiltrates in the treated skin. Higher concentration of the test article were associated with higher severity of these cutaneous changes compared to controls, and a low incidence of the formation of erosion/ulcers at the treated site. Efinaconazole 10% solution applied intratympanically to the guinea pig middle ear caused significant middle ear inflammation and hearing impairment. In dermal toxicity studies, efinaconazole was well tolerated in minipigs at doses up to 150-200 mg /kg/day. Slight to moderate skin reactions were noted macroscopically and microscopically in all test article groups and vehicle control and consisted of hyperkeratosis, acanthosis and localized inflammation. These skin effects were attributed to the vehicle and were not considered adverse due to the mild severity of changes. A 2-year dermal carcinogenicity study in mice was conducted with daily topical administration of 3%, 10% and 30% efinaconazole solution. Severe irritation was noted at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinaconazole. The high dose group was terminated at week 34 due to severe skin reactions. No drug-related neoplasms were noted at doses up to 10% efinaconazole solution (248 times the MRHD based on AUC comparisons). In a pre- and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day efinaconazole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryofetal toxicity (increased pre-natal pup mortality, reduced live litter sizes and increased post-natal pup mortality) was noted at 25 mg/kg/day. No embryofetal toxicity was noted at 5 mg/kg/day (17 times the MRHD based on AUC comparisons). No effects on post-natal development were noted at 25 mg/kg/day (89 times the MRHD based on AUC comparisons). Subcutaneous doses of 1, 5, and 10 mg/kg/day efinaconazole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rabbits. In the presence of maternal toxicity, there was no embryofetal toxicity or malformations at 10 mg/kg/day (154 times the MRHD based on AUC comparisons). Efinaconazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay). /LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. The high doses were the maximum tolerated doses, based on increased frequency of severe injection site reactions and a 17% average lower

body weight in males compared to controls. No target organs of toxicity were identified at any dose level. Administration of the propylene glycol vehicle at 2 mL/kg over 6 months was not well tolerated and resulted in mortalities in all groups. Vehicle-related effects included severe dermal clinical signs, and gross and microscopic pathology findings at the injection sites. Early death in several efinaconazole-treated rats was attributed to spinal cord necrosis and urinary tract disease; these lesions also were noted in control rats and were attributed to the spread of injection site reactions (necrosis, abscessation). The NOAEL was determined to be 10 mg/kg/day in both male and female rats which had an exposure of 70 folds or more for efinaconazole and metabolite H3 as compared to human exposure levels.
- Reproductive toxicity: No data available.
- STOT-single exposure: /LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. The high doses were the maximum tolerated doses, based on increased frequency of severe injection site reactions and a 17% average lower body weight in males compared to controls. No target organs of toxicity were identified at any dose level. Administration of the propylene glycol vehicle at 2 mL/kg over 6 months was not well tolerated and resulted in mortalities in all groups. Vehicle-related effects included severe dermal clinical signs, and gross and microscopic pathology findings at the injection sites. Early death in several efinaconazole-treated rats was attributed to spinal cord necrosis and urinary tract disease; these lesions also were noted in control rats and were attributed to the spread of injection site reactions (necrosis, abscessation). The NOAEL was determined to be 10 mg/kg/day in both male and female rats which had an exposure of 70 folds or more for efinaconazole and metabolite H3 as compared to human exposure levels.
- STOT-repeated exposure: /HUMAN EXPOSURE STUDIES/ Onychomycosis is a chronic condition that often requires long-term management to eradicate the causative fungus, allow a healthy nail to grow, and prevent relapse. As a successful outcome depends highly on patient adherence with treatment, a low risk of periungual skin irritation with topical medication is clinically relevant. /The purpose of this research was/ to study the potential for efinaconazole 10% solution and its corresponding vehicle to induce delayed contact skin sensitization and evaluate its skin irritation potential. Efinaconazole 10% solution and its vehicle were studied in 239 healthy volunteers for the potential to induce contact skin sensitization. This included a series of induction, challenge, and re-challenge phases. An additional 21-day cumulative irritation study was undertaken in 35 healthy volunteers to compare three concentrations of efinaconazole (1%, 5%, and 10%), vehicle, and positive/negative controls. There was no evidence of induced contact sensitization under occlusive, semi-occlusive, and open (open rub-in) applications of efinaconazole 10% solution. Efinaconazole 1%, 5%, and 10% solutions have mean cumulative irritancy indices of 1.12, 1.26, and 1.18, respectively, where a range of >0 to =1 is classified as "mildly irritating." Results were comparable to vehicle (1.04). Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in the studies completed. /LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ In 13 week dermal toxicity in mice, the systemic exposure to efinaconazole was much higher as compared to minipig. In this study an increase in liver weight and minimal to mild panlobular hepatocellular hypertrophy was observed 30% IDP-108, the local application of IDP-108 and/or the vehicle alone resulted in higher incidences of hyperkeratosis, epidermal hyperplasia, and mononuclear infiltrates in the treated skin. Higher concentration of the test article of 10% and 30% IDP-108 were associated with higher severity of these cutaneous changes compared to controls, and a low incidence of the formation of erosion/ulcers at the treated site. The NOAEL, established by the 30% strength which had an exposure of 700 folds or more for efinaconazole as compared to human exposure levels.
- Aspiration hazard: No data available.

Likely routes of exposure
- No data available.

Symptoms related to the physical, chemical and toxicological characteristics

- IDENTIFICATION AND USE: Efinaconazole is used as antifungal agent. It is indicated for the topical treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes. HUMAN EXPOSURE AND TOXICITY: Efinaconazole 10% solution did not cause contact sensitization and induced only minimal skin irritation in human studies. ANIMAL STUDIES: Efinaconazole was generally well tolerated in rats with repeated daily doses of up to 30 (males) and 40 (females) mg/kg. In 13 week dermal toxicity in mice, an increase in liver weight and minimal to mild panlobular hepatocellular hypertrophy was observed, the local application of the drug and/or the vehicle alone resulted in higher incidences of hyperkeratosis, epidermal hyperplasia, and mononuclear infiltrates in the treated skin. Higher concentration of the test article were associated with higher severity of these cutaneous changes compared to controls, and a low incidence of the formation of erosion/ulcers at the treated site. Efinaconazole 10% solution applied intratympanically to the guinea pig middle ear caused significant middle ear inflammation and hearing impairment. In dermal toxicity studies, efinaconazole was well tolerated in minipigs at doses up to 150-200 mg /kg/day. Slight to moderate skin reactions were noted macroscopically and microscopically in all test article groups and vehicle control and consisted of hyperkeratosis, acanthosis and localized inflammation. These skin effects were attributed to the vehicle and were not considered adverse due to the mild severity of changes. A 2-year dermal carcinogenicity study in mice was conducted with daily topical administration of 3%, 10% and 30% efinaconazole solution. Severe irritation was noted at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinaconazole. The high dose group was terminated at week 34 due to severe skin reactions. No drug-related neoplasms were noted at doses up to 10% efinaconazole solution (248 times the MRHD based on AUC comparisons). In a pre- and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day efinaconazole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryofetal toxicity (increased pre-natal pup mortality, reduced live litter sizes and increased post-natal pup mortality) was noted at 25 mg/kg/day. No embryofetal toxicity was noted at 5 mg/kg/day (17 times the MRHD based on AUC comparisons). No effects on post-natal development were noted at 25 mg/kg/day (89 times the MRHD based on AUC comparisons). Subcutaneous doses of 1, 5, and 10 mg/kg/day efinaconazole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rabbits. In the presence of maternal toxicity, there was no embryofetal toxicity or malformations at 10 mg/kg/day (154 times the MRHD based on AUC comparisons). Efinaconazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay).

SECTION 12: Ecological information

Not available

SECTION 13: Disposal considerations

Not available

SECTION 14: Transport information

Not available

SECTION 15: Regulatory information

Not available

SECTION 16: Other information

Not available

DISCLAIMER

This MSDS is system-generated. Please verify and confirm all data, statements, and values with the Support Team before use or distribution.