CINACALCET HYDROCHLORIDE

API MASS BALANCE | MANUFACTURING PROCESS FLOW

Source-based technical illustration | All five worksheets | One-page A2

TECHNICAL REVIEW

Material balance / Flow chart / CC

Raw materials / MOLES

TOTAL RECORDED INPUT	TOTAL RECORDED OUTPUT	FINAL CINACALCET HCL	REPORTED YIELD
96.86 kg	96.86 kg	1.00 kg	27.47%
Detailed balance	Detailed balance	Source: output row	Calculated: 55.56%

MANUFACTURING PROCESS FLOW

Unquantified Stage-A transfer is shown as a process step, not a recovered output

01 Reaction — Starting material + amine
02 Reduction — NaBH4 + methanol
03 Work-up — Ethyl acetate + water
04 Distillation — Solvent recovery
05 Stage-A — Intermediate
06 Reaction — HCl + ethyl acetate
07 Filtration — Filtrate separation
08 Drying — Final API: 1 kg

RAW MATERIAL / CHARGE COMPOSITION

SR.	RAW MATERIAL	QTY (kg)
01	3- 3-(trifluoromethyl)phenyl propionaldehyde	2.02
02	(R)- (+)-1-(1-Naphthyl)ethylamine	1.36
03	Methylene dichloride	8.00
04	Sodium Borohydride	0.28
05	Methanol	8.00
06	Ethyl acetate	48.00
07	Dilute HCl	1.20
08	**Water (listed in material balance; excluded from CC)**	**28.00**

TOTAL CHARGE / INPUT **96.86 kg**

CC: 68.86 kg + Water: 28.00 kg

MASS BALANCE: RECOVERIES & OUTPUTS

SR.	MATERIAL / STREAM	QTY (kg)
01	Aqueous layer to ETP	35.00
02	Evaporation loss	1.36
03	Ethyl acetate distillate	35.00
04	Evaporation loss	2.30
05	Filtrate (disposition to confirm)	19.20
06	Evaporation loss	1.50
07	Evaporation loss	1.50
08	**Cinacalcet HCl (final API)**	**1.00**

TOTAL RECORDED OUTPUT **96.86 kg**

Includes solvent recovery, effluent, filtrate and API

MOLES & PROPOSED MATERIAL CONSUMPTION

NO	INPUT COMPONENT	MW	kg	MOLES	RATIO	EXIST MT/d	PROPOSED MT/d	TOTAL MT/d
01	3- 3-(trifluoromethyl)phenyl propionaldehyde	218.17	2.02	9.26	1.00	0.000	0.140	0.140
02	(R)- (+)-1-(1-Naphthyl)ethylamine	171.24	1.36	7.94	0.90	0.000	0.094	0.094
03	Methylene dichloride	-	8.00	-	-	0.000	0.555	0.555
04	Sodium Borohydride	37.83	0.28	7.40	0.80	0.000	0.019	0.019
05	Methanol	-	8.00	-	-	0.000	0.555	0.555
06	Ethyl acetate	-	48.00	-	-	0.000	3.333	3.333
07	Dilute HCl	-	1.20	-	-	0.000	0.083	0.083

Consumption figures are transcribed from MOLES sheet (MT/day); not independently verified.

RECOVERY / EFFLUENT / EMISSIONS

Recovered ethyl acetate	35.00 kg
Aqueous effluent (ETP)	35.00 kg
Fugitive emissions (source)	6.66 kg
Solid waste (source)	Nil
Evaporation rows (sum)	6.66 kg

Filtrate of 19.20 kg: disposition not specified.

SOURCE VERIFICATION / GMP RECONCILIATION ITEMS

REVIEW BEFORE APPROVAL

01 Yield discrepancy
Reported 27.47%; 1.00 / 1.80 kg theoretical = 55.56%. Confirm yield basis.

02 CC and balance basis
CC charges 68.86 kg; balance adds 28.00 kg water. Total 96.86 kg.

03 Filtrate disposition
19.20 kg filtrate is recorded as an output; waste/reuse destination is unspecified.

04 Scale / consumption basis
MOLES MT/day and waste MT/day figures need a consistent production-day basis.

Source: 6-Cinacalcet HCl.xlsx | material balance sheet, Flow chart, CC, Raw materials, MOLES.

Technical illustration only: verify yield, filtrate disposition and production basis before controlled GMP use.

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